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Community Health Associated with Arsenic in Drinking Water in Millard County, Utah

Utah Dept. of Health, Salt Lake City

Prepared for

Health Effects Research Lab.
Cincinnati, OH

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COMMUNITY HEALTH ASSOCIATED WITH ARSENIC IN DRINKING WATER IN MILLARD COUNTY, UTAH

by

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This study evaluates the health effects of arsenic in drinking water at levels approximately four times the maximum allowed by the National Interim Primary Drinking Water Regulations. Physical examinations of 250 people included evaluating dermatological and neurological health, sampling hair and urine for arsenic content and testing for anemia. Water consumption estimates were used to estimate arsenic ingestion.

A clear relationship was shown between the amount of arsenic consumed and the amount of arsenic present in hair and urine samples. Dermatological signs compatible with arsenic exposure were rare and, when found, were scattered singly among both exposed and control participants rather than being clustered as multiple signs on individuals with higher arsenic exposure. Anemia was not found significantly more often among exposed participants. Nerve conduction slowing did not correlate significantly with arsenic exposure levels. Typical signs and symptoms of arsenic intoxication were not found in any of the study participants.

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FOREWORD

The primary mission of the Health Effects Research Laboratory is to provide the EPA Regulatory Offices with human health assessments for populations exposed to environmental contaminants. This information is used in the Agency's standard setting procedures to ensure that man is protected from significant adverse health effects.

The objectives of the investigation reported herein were to assess the human health implications of consuming drinking water contaminated with arsenic. The investigation involved comparisons of body burden levels, physical examination results, and cancer incidence and mortality rates between a population exposed to 0.18 to 0.21 mg/l of arsenic in their drinking water and a comparison population not so exposed. Levels of arsenic in hair and urine clearly reflect the levels of arsenic in the drinking water. However, no significant differences were observed between the health or mortality experiences of the arsenic exposed and comparison populations.

The results of this study fail to demonstrate significant health effects associated with exposures to moderate levels of waterborne arsenic. However, since the study was relatively small (145 exposed and 105 comparison participants), these results must be considered as only part of the evidence necessary for assessing the human health implications of waterborne arsenic exposure.

James B. Lucas
Acting Director
Health Effects Research Laboratory

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ABSTRACT

This study evaluates the health effects of arsenic in drinking water at levels approximately four times the maximum allowed by the National Interim Primary Drinking Water Regulations. Physical examinations of 250 people included evaluating dermatological and neurological health, sampling hair and urine for arsenic content and testing for anemia. Water consumption estimates were used to estimate arsenic ingestion.

Study participants came from a homogeneous, stable population with minimum influence from cigarette smoking due to the predominantly "Mormon" lifestyle of Millard County, Utah where they resided. The 145 "exposed" participants came from Hinckley and Deseret where drinking water arsenic content averaged 0.18 and 0.21 mg/l respectively. A matched control group of 105 participants was selected from neighboring Delta where drinking water arsenic averaged 0.02 mg/l.

A clear relationship was shown between the amount of arsenic consumed and the amount of arsenic present in hair and urine samples. Dermatological signs compatible with arsenic exposure were rare and, when found, were scattered singly among both exposed and control participants rather than being clustered as multiple signs on individuals with higher arsenic exposure. Anemia was not found significantly more often among exposed participants. Nerve conduction slowing did not correlate significantly with arsenic exposure levels. Typical signs and symptoms of arsenic intoxication were not found in any of the study participants.

Cancer incidence and cancer death rates did not suggest an excess of cancer in the exposed community. In general, the exposed participants appeared to be as healthy as control participants. No adverse health effects could be confirmed by this study for people exposed to arsenic in drinking water at four times the maximum allowed by current standards.

This report was submitted in fulfillment of Grant No. R-804-617-01 by the Utah State Department of Health under the sponsorship of the U.S. Environmental Protection Agency. This report covers a period from November 1, 1976 to January 31, 1980, and work was completed as of February 29, 1980.

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The initial planning of the study received considerable support from Dr. Alan G. Barbour and Dr. Taira Fukushima of the Disease Control Branch of the State Division of Health and is gratefully acknowledged.
Many community leaders in West Millard County were instrumental in soliciting excellent community support for this study. Especially helpful were Leigh R. Maxfield, Merlin Christensen and Willard Wells Wood of Delta; Walter Ekins of Hinckley, and Orin Allred of Deseret.
To Dr. Kenneth M. Topham and the Millard County School District we extend special thanks for making the Delta High School available for conducting the physical examinations.
A critical review of the findings of this study by Dr. Joseph L. Lyon of the University of Utah Medical Center, Department of Family and Community Medicine, was especially useful in improving the presentation of the data and was sincerely appreciated.
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SECTION 1

INTRODUCTION

BACKGROUND

Arsenic is a common mineral widely distributed in the environment. In various chemical combinations, arsenic is notorious primarily for its acute toxicity (Lisella et al., 1972). Epidemiological evidence has accumulated to show that arsenic consumed in drinking water has been responsible for specific signs and symptoms of illness, and even death (Zaldiver, 1974 and Tseng et al., 1968). Since 1900, limits or standards have been set to control the amount of arsenic that can be permitted in food and water (Lisella et al., 1972). In the United States the "Interim Primary Drinking Water Regulations" allow a maximum of 0.05 mg. of arsenic per liter of drinking water (Environmental Protection Agency, 1976). This U.S. Standard is unchanged from the U.S. Public Health Service Standard of 1962.

While several studies suggest that specific signs, symptoms, and medical problems may be associated with too much arsenic in drinking water, they also show a number of conspicuous disparities in the kinds of signs and symptoms recorded depending upon where the various episodes were studied.

Tseng, et al., (1968) reported a major episode of waterborne arsenic poisoning in an area on the southwest coast of Taiwan. The predominant signs, symptoms, and illnesses reported from this study were hyperpigmentation, keratoses, skin cancer, and a circulatory disorder locally known as "blackfoot disease." The average concentration of arsenic in the well waters consumed by this population was 0.6 mg/liter. Water from the wells was used for more than 45 years. This study showed the prevalence rate of skin cancer to increase in direct proportion to the arsenic content of the well water.

In the city of Antofagasta, Chile (Zaldivar, 1974) an investigation was made into reported chronic arsenic poisonings. The source of arsenic was the drinking water supply. The mean concentration of arsenic in this water was determined to be 0.8 mg/liter. Children (0-15 years of age) were the predominant patients. Among the signs and symptoms recorded from this population were weight loss, diarrhea, general debilitation, anorexia, and scaling of the skin. Over 80 percent of the affected population had abnormal skin pigmentation, many had hyperkeratosis of palms and soles. There was a high frequency of bronchopulmonary disease, especially bronchiectasis. There were also several cases of ischemia and myocardial infarction, also mesenteric thrombosis.

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Vallee, et al., (1960) reported that polyneuritis and motor-palsies may be the only manifestations of chronic exposure to arsenic. Heyman, et al., (1956) investigated 41 cases of arsenical polyneuropathy. A number of the cases had more than chronic exposures. For these patients the onset was sudden and dramatic. The first signs in those patients with chronic exposure were weakness, prostration, muscular aching, and personality changes. Cutaneous manifestations were recorded after six weeks. Large areas of skin over the trunk and arms became highly pigmented. Hyperkeratotic scaling developed especially over hands and soles. Some of the patients developed white transverse bands on their fingernails (Mee's Lines). The onset of symptoms of neuropathy was characterized by the appearance of numbness, tingling, and sensations of "pins and needles" in the feet. Sensory examinations showed a decrease in touch, pain, and temperature sensations in their hands, feet, and lower legs in a symmetrical "stocking-glove" distribution. In more severe cases other signs and symptoms were recorded.

Tsuchiya (1977) summarized a number of arsenic studies in Japan. He called attention to abnormal electromyographic findings in residents living near mining and smelting operations where copper and arsenic trioxide were produced. Interest has developed in the possible prolongation of nerve conduction velocities due to the absorption by the body of certain toxic metallic ions.

Mizuta et al.,(1956) and Miyata et al., (1970) [as reported by Tsuchiya (1972)] studied arsenic poisonings resulting from consumption of contaminated soy sauce and milk. Anemia was reported as a frequent abnormality exhibited by the victims.

Arsenic has been associated with diseases of the cardiovascular system in a number of epidemiological studies. Early in 1901, Reynolds examined 500 patients suffering from arsenical poisoning. Cardiac and hepatic signs and symptoms were recognized in approximately 25 percent of the patients. Thirteen deaths were attributed to congestive heart failure. Later Borgono and Greiber (1972) and Zaldivar (1974) reported on dermatological manifestations and deaths especially among children. Over 70 percent of the cases were children 0 to 15 years of age. Deaths were reported due to thrombosis of mesenteric and brain arteries, narrowing of coronary arteries, and/or myocardial infarction.

An association of arsenic and cancer has also been reported in some of the studies. Rosset (1958) reported keratoses associated with carcinomas of the internal organs. Sommers and McManus (1953) reported a study where cancer of skin and internal organs were associated with arsenical poisoning. However, conclusive evidence for such a relationship is not available.

Not all studies of people with arsenic exposure from drinking water showed evidence of health effects. Morton et al., (1976) expressed disappointment to have found no association between drinking water arsenic levels of approximately 0.100 mg/l in Lane County, Oregon and skin cancer incidence. Dermatologists of that area seldom saw arsenical keratosis or hyperpigmentation despite their awareness of the widespread potential exposure to arsenic. Goldsmith et al. (1972) evaluated the health significance of 0.100 to 1.000

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mg/l of arsenic in drinking water in Lassen County, California. They concluded that although arsenic levels in drinking water above 0.05 mg/l increased arsenic levels in the hair, they could find no evidence of any specific illness associated with elevated arsenic levels.

It is evident from the literature that cutaneous lesions (hyperpigmentation, keratoses, and some skin cancers) are the more consistent signs of chronic arsenic exposure. With reference to these studies the National Academy of Science (Arsenic 1977) observed, "It should be noted that many studies of populations 'at risk' have failed to evaluate cutaneous changes adequately. Proper examinations of the skin of people subjected to chronic low-dose arsenic exposure have the potential of providing valuable information related to dose and duration of exposure necessary to cause changes in given populations. In a word, these benign skin lesions may be regarded as sensitive indexes of exposure to an agent that has potentially serious consequences."

Since exposure to arsenic in drinking water has produced such varied results, continued research and study are necessary in order to more accurately assess the health impact of arsenic on the residents of a community where the drinking water contains a level of arsenic that exceeds the maximum permitted by the National Standards (Fowler, 1977).

Since an adequate animal model for arsenic intoxication studies has not been found, there is a need for studies to be performed on populations that are inadvertently exposed to arsenic in their drinking water (National Academy of Science, 1977). The residents of Hinckley and Deseret, (Millard County, Utah) are among those inadvertently exposed populations. The Hinckley community's drinking water supply contains a level of arsenic (mean = 0.180 mg/liter) approximately four times the maximum limit permitted by the National Standards. Deseret residents have only private wells which contain arsenic in the range of 0.053 to 0.750 mg/liter. (Only residents of Deseret with wells exceeding 0.150 mg/l were included in this study.)

This West Millard County area and its residents provided an excellent opportunity to study the health effects of drinking water containing concentrations of arsenic which exceed the National Standard. The drinking water in Hinckley and Deseret exceeded the level of arsenic permitted by the Standard while arsenic in the water supply of Delta was well within the limits of the Standard (mean = 0.019 mg/l). The residents of all three communities are part of the same stable, homogenous, predominantly "Mormon" population. The study of these communities was undertaken in 1976 by the Utah State Division of Health under a grant from the United States Environmental Protection Agency.

OBJECTIVE

The objective of this study was to test the following hypothesis:

> A population which consumes drinking water containing levels of arsenic which exceed National Drinking Water Standards by approximately four to eight times will show more signs and symptoms

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of chronic arsenic poisoning than a matched control population which consumes drinking water with minimal arsenic content.
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SECTION 2

METHODS AND PROCEDURES

STUDY DESIGN

This study was designed to test the hypothesis and evaluate the health effects of consuming arsenic in drinking water by the following methods:

1. Assessment of environmental exposure to arsenic.

   a. Environmental sampling in each community to document arsenic exposure potential from drinking water and airborne particulates.

   b. Estimating drinking water's contribution to arsenic consumption by obtaining answers to a water consumption questionnaire from each study participant.

   c. Measuring levels of arsenic in hair and urine samples of participants from each community to show levels of arsenic uptake from the environment.

2. Assessment of health status.

   a. Examining participants for dermatological signs of chronic arsenic poisoning, such as hyperpigmentation, keratoses, vascular changes, and skin cancers.

   b. Determining nerve conduction velocities and performing neurological examinations on participants.

   c. Measuring hematocrits to identify anemia among participants.

   d. Evaluating community death rates and cancer incidences.

STUDY SUBJECTS

Description of Study Communities

The West Millard County, Utah, area is located near the center of a large desert valley. The land slopes to the southwest; however, the valley is so large it makes the land appear flat. The area is rural with agriculture, the primary source of livelihood.

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The inhabitants of the area are over 95 percent caucasian. The early Mormon settlers of the area were predominantly English with a small number from Scandinavia. In the 1860s and 1870s, they settled in Deseret. As their numbers increased, they moved out to form other communities, including Hinckley, and later Delta. Many of the families in these stable communities are related to each other.

The drinking water supply for the area comes from deep wells. Two communities, Hinckley and Delta, have developed public drinking water systems. The residents of smaller surrounding communities, such as Deseret, obtain their drinking water from individual wells located near the family home.

Arsenic content of groundwater in this area tends to increase toward the southwest (See Figure 1). Delta, the larger of the three study communities (population = 1610), is situated in the northeast of Millard County and its drinking water wells contain very little arsenic (less than 0.025 mg/l). Hinckley (population = 400), which is west-southwest of Delta, discovered arsenic levels of approximately 0.180 mg/l in water from its new culinary well which was completed in 1968. Prior to 1968 Hinckley residents consumed water from private wells. Of the five private wells available for testing in Hinckley during the study, the average concentration of arsenic was 0.178 mg/l (range 0.100 - 0.250). Private wells serving families of Deseret (population = 210) ranged from 0.053 to 0.750 mg/l with the higher concentrations of arsenic tending to be found in wells toward the southwest.

Selection of Exposed Participants

Exposed participants were selected from residents of the Hinckley and Deseret areas where their drinking water was tested and known to contain at least 0.150 mg/l of arsenic. Males and females, five years of age or older and current residents of the arsenic exposed communities for a minimum of five years, were selected as exposed participants. The majority of the eligible participants had lived in their communities most of their lives. All qualified individuals were included in the study, except for a few who (because of apparent antipathy toward government) refused the invitation to participate.

Selection of Control Participants

Control participants were selected from the residents of Delta where the drinking water supply contains less than 0.025 mg of arsenic per liter of water. Residents of Delta who had lived part of their lives in Hinckley, Deseret, or surrounding areas where the drinking water contained a level of arsenic that exceeded the National Standard of 0.05 mg / liter of water were not selected as control participants.

Control participants were screened for exposure to arsenic through use of arsenic-containing pesticides or other arsenic-containing chemicals. No control participants were found to have this type of arsenic exposure.

The age and sex distribution of the control population was made to reflect the age and sex distribution of the exposed population (see Tables 1 and 2). Since the eligible control population was larger than the exposed

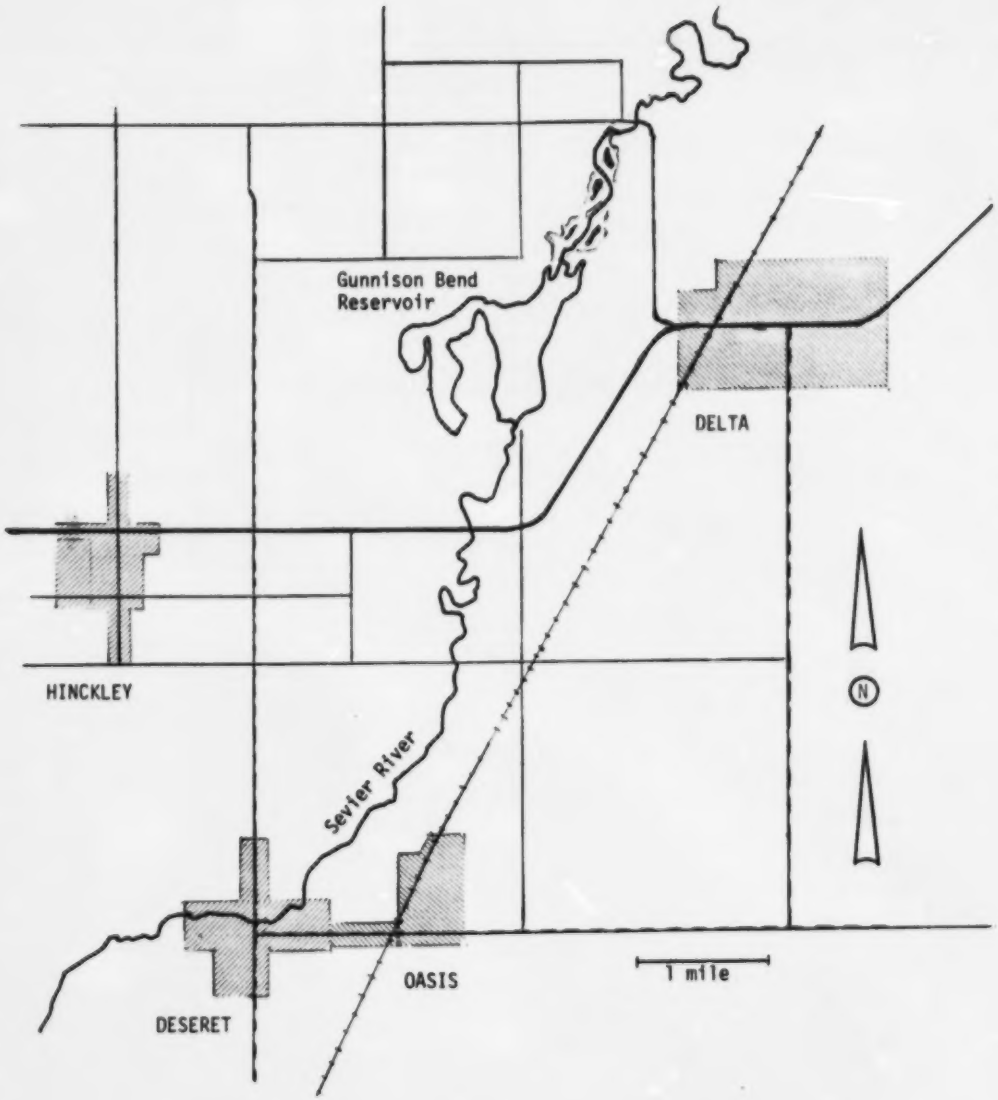

FIG. 1. Map of West Millard County, Utah, showing the geographic relationship of the control community (Delta) to the arsenic exposed communities (Hinckley and Deseret).

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population, control candidates were grouped by age categories and a number was given to each. Control participants were then chosen by random number selection from within age categories.

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Recruitment of Participants

After obtaining cooperation of community leaders, public meetings were held in Hinckley and Deseret to explain the need for a study of arsenic health effects and to solicit support. People attending the meetings voted to support the study.

A card file (Figure 2) of families living in all three study communities was prepared from various sources including the telephone directories, school, and church records.

Participants were recruited by families. Families listed in the card file were visited by study representatives and those willing to participate were recruited into the study. Information required to determine eligibility to participate in the study was obtained through the administration of a brief questionnaire entitled "Household Census and Water Survey" (Figure 3). People meeting the eligibility criteria outlined above were selected to participate in the study.

A few families and individuals from the exposed communities (33 total people) were antagonistic toward the study and refused to participate due to antipathy toward government. We could not determine how many of these 33 people would have met the eligibility criteria had they been willing to participate in the study. Table 1 shows that of the 223 persons determined to be eligible for the exposed group, we were successful in scheduling 83 percent for physical examinations. Although all adults over 30 years old were scheduled for physical examinations, we encountered reluctance when we tried to schedule some young adults and youth. A few persons in all age groups failed to keep their appointments for physical examinations. Sixty-five percent of the eligible exposed group were actually evaluated by physical examination.

Table 2 shows similar information for the control group. Of the 226 selected, 69 percent were successfully scheduled for physical examinations. As with the exposed group, some did not keep their appointments. Forty-six percent of the selected control group were actually evaluated by physical examination.

Table 3 shows the final distribution of study participants. The match between control and exposed groups remained quite close. Our concern for balance within the study population was directed toward balance between exposure groups. We wanted the control population to mirror the age and sex distribution of the exposed population. We attempted to analyze possible imbalances in our study population using a multiway frequency table analysis from BMDP (Brown, 1979). This analysis for balance showed that the available exposed population was not perfectly balanced across age categories, but balance was achieved between exposure groups.

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HOUSEHOLD CENSUS AND DATA CARD - ARSENIC STUDY

NAME-HEAD OF HOUSEHOLD _____ PHONE _____

ADDRESS _____

CITY _____ ZIP CODE _____

OCCUPATION _____ DATE _____

NAME	SEX	Date of Birth MO YR	SCHOOL	GRADE	CLASS
Father					
Mother					
Remarks					

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DRINKING WATER-RESIDENCE INFORMATION

Main Source of Family's Drinking Water _____

Additional Source _____

Towns & Cities of Family Residence (Beginning with Present)

Town-City Year

_____

_____

_____

_____

FIG. 2. Data card for file of potential participants in the arsenic study.

HOUSEHOLD CENSUS AND WATER USE SURVEY - ARSENIC STUDY 24 28 294

Date _____ Name Head of Household _____

Phone _____ Address _____

Community _____ Zip Code _____

Family Census and Residence Data:

Nu	Name of Family Member	Sex	Date of Birth	Have you Always Lived in This Community? Yes	No	IF NO Explain: Residence in This Community — Current Nu Yrs	Total Nu Yrs	Residence Outside This Community — Town or City	Any History of Arsenic use?
1				☐	☐				
2				☐	☐				
3				☐	☐				
4				☐	☐				
5				☐	☐				
6				☐	☐				
7				☐	☐				
8				☐	☐				
9				☐	☐				
				☐	☐				

Water Source Data:

Where does the Tap water in your home come from?

☐ Community (Public) Supply ☐ Private Well

☐ Other _____

How Long Have You Used Water From This Source?

☐ Less than One Year

☐ 1 to 5 yrs _____ Years

☐ 5 yrs or More _____ Years

Additional Information:

FIG. 3. Questionnaire to determine eligibility of potential participants for the arsenic study.

participants in the age category 13-20. Nonetheless, this characteristic was not significantly different between exposure groups. That is, the control population mirrored the age (and sex) patterns of the exposed population even though there were significantly fewer control participants (P = .005). No significant differences between control and exposured participants were found for age categories ("P"s ranging from .944 to .103) or sex (P = .904).

Table 1. Eligible exposed participants (from Hinckley and Deseret) showing percent successfully scheduled for physical examinations and the percent actually examined.

Age Group	Total number eligible		Percent scheduled		Percent examined	
	Male	Female	Male	Female	Male	Female
7-12	24	14	42%	43%	42%	43%
13-20	28	27	68%	78%	43%	52%
21-30	8	7	88%	86%	63%	57%
31-40	11	14	100%	100%	82%	79%
41-50	12	13	100%	100%	50%	100%
51-60	14	13	100%	100%	79%	100%
61-70	10	11	100%	100%	80%	82%
71+	8	10	100%	100%	75%	80%
Totals	115	108	79%	86%	58%	72%
Grand Total	223		83%		65%	

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Table 2. Randomly selected control participants (from Delta) showing percent successfully scheduled for physical examinations and the percent actually examined.

Age Group	Total number selected		Percent scheduled		Percent examined	
	Male	Female	Male	Female	Male	Female
7-12	24	18	25%	22%	25%	11%
13-20	30	29	57%	62%	20%	45%
21-30	11	9	73%	78%	36%	67%
31-40	14	19	86%	95%	57%	68%
41-50	16	12	100%	92%	44%	58%
51-60	9	13	100%	77%	89%	69%
61-70	9	8	89%	100%	67%	75%
71+	3	2	100%	100%	67%	100%
Totals	116	110	68%	71%	41%	53%
Grand Total	226		69%		46%	

Table 3. Age and sex distribution of study participants from control (Delta) and exposed (Hinckley and Deseret) communities.

Ages	Control				Exposed			
	Male	%	Female	%	Male	%	Female	%
7-12	6	12.8	2	3.5	10	14.9	6	7.7
13-20	6	12.8	13	22.4	12	17.9	14	17.9
21-30	4	8.5	6	10.3	5	7.5	4	5.1
31-40	8	17.0	13	22.4	9	13.4	11	14.1
41-50	7	14.9	7	12.1	6	9.0	13	16.7
51-60	8	17.0	9	15.5	11	16.4	13	16.7
61-70	6	12.8	6	10.3	8	11.9	9	11.5
71+	2	4.3	2	3.5	6	9.0	8	10.3
Totals	47	44.8	58	55.2	67	46.2	78	53.8
Grand Total	105				145			

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ASSESSMENT OF EXPOSURE TO ENVIRONMENTAL ARSENIC

Environmental Sampling for Arsenic

Monthly drinking water samples were obtained from the Hinckley community drinking water well (May 1976 - May 1977). The purpose was to assess possible seasonal variation in arsenic content of Hinckley water, and to compute a better average arsenic content value. Delta community drinking water was sampled similarly during the same time period and tested for arsenic content. Some months each of the three Delta wells were sampled individually, while on other months a mixed sample from the Delta water system was taken.

The families in Deseret had no community water system, so individual private wells were sampled and tested to evaluate arsenic levels. Prior to selecting Deseret residents for participation in the arsenic study, each potential participant's home drinking water well was sampled and tested for arsenic content.

An air monitoring station was established near Delta to measure total suspended particulates on a daily basis for a year (July 1977 - June 1978). Each week the filter with the heaviest particulate load was set aside for arsenic content analysis. The purpose was to obtain an estimate of the amount of airborne arsenic in that dry desert region on the chance that airborne arsenic might confound the study.

Collecting Hair and Urine Samples

Early in the study (May, 1977) 119 hair and 153 urine samples were collected from school-age children to document arsenic body-burden differences between Hinckley and Delta. Bottles for urine and envelopes for hair were delivered to cooperating families by study representatives. Participants were instructed to collect a first morning void of urine and to take hair samples from hair growing closest to the skin. There was some evidence that our collection instructions were not consistently followed. Resulting hair and urine samples were picked up from families and delivered to the laboratory for analysis.

Later (August, 1978), as part of the physical examination, 185 hair and 234 urine samples were obtained. Each participant in the physical examination was given a urine sample bottle. Most produced a urine sample at that time. No attempt was made to account for possible diurnal variation in urine concentrations. A few took the sample bottle home with them, but generally did not return with a urine sample. Table 4 shows the number of participants from each study community and the number of urine and hair samples received.

Each participant in the physical examination was given a self-addressed, postage-paid envelope with his name on it. Each was instructed to place a quantity of hair from their next haircut in the envelope and mail it to the address on the envelope (the study headquarters). Hair samples began arriving at the office almost immediately after the physical examination and continued for several months. Almost 75 percent of the participants sent in hair samples, which was considered an excellent return. Most of the people

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who failed to send hair samples were from the control community. Table 5 shows the age and sex distribution of participants who sent in hair samples.

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Table 4. Number of physical examination participants from each study community showing number of hair and urine samples received.

Community	Number of participants	Number of samples collected	
		Urine	Hair
Control (Delta)	105	99	68
Exposed communities	145	135	117
Hinckley	102	95	80
Deseret	43	40	37
Total	250	234	185

Table 5. Percentage of participants who sent in hair samples by age category, sex, and exposure group.

Age Category	Control Group		Exposed Group	
	Male	Female	Male	Female
7-12	67%	100%	90%	50%
13-20	33%	62%	83%	64%
21-30	75%	50%	80%	100%
31-40	63%	46%	78%	64%
41-50	57%	86%	83%	85%
51-60	86%	89%	82%	85%
61-70	67%	67%	88%	89%
70+	100%	50%	100%	78%
% of Total	64%	66%	85%	77%
% of Grand Total	65%		81%	

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Laboratory Methods for Arsenic Determinations

Analyses for arsenic in water, urine, and hair samples, and on the air sample filters were done by the Utah State Division of Health, Bureau of Laboratories. The water was analyzed by the automated sodium borohydrate method using a tube furnace.

After specific gravity was measured for each urine sample, a 25 ml aliquot was withdrawn for ashing. The samples were ashed using a mixture of nitric, perchloric, and sulphuric acids. The ash was dissolved in water, diluted, and analyzed with the automated hydride method. Urinary arsenic levels were not adjusted for specific gravity.

Hair samples were washed with residue-free detergent, rinsed thoroughly with distilled water and dried at room temperature overnight. A portion (0.1 to 1.0 g) was weighed and ashed using a mixture of nitric, perchloric, and sulphuric acids. The ash was dissolved in water and diluted to 100 ml. The samples were analyzed using the automated hydride method.

High volume air samples were collected on 8 x 10 inch glass fiber filters. The filters were cut into strips 3/4 x 8 inches which are equal to 1/12 of the entire sample. The strips were heated in 3 N nitric acid for 30 minutes. After cooling, the solution was decanted into Phillips beakers. Distilled water was added to the beakers containing the strips and placed in the ultrasonic vibrator to allow the nitric acid trapped in filter to diffuse into the water. These washings were added to the first decanted solution. Concentrated sulfuric acid was added to the combined solutions. The resulting solution was evaporated to fumes of sulfuric acid. After cooling, distilled water was added to dissolve the ash and dilute the material to 25 ml. The resulting samples were analyzed by the automated borohydride method.

In general, the following control procedures were followed for every 20 samples:

1. At least one blank.
2. Four or more standards ranging from 5 to 40 µg/liter arsenic.
3. At least one "spiked" sample.
4. At least two duplicate samples.
5. Unused glass fiber filters were cut the same way as the high volume filters and run for controls. (0.3 µg of arsenic average on unused 8"x10" filters.)

Estimating Arsenic Exposure from Drinking Water

When study participants reported for their physical examination, they were asked to complete a "Water and Beverage Consumption Questionnaire" (Figure 4). As they filled out the questionnaire an assistant showed him or her an eight ounce water glass and asked for consideration of the various

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REPLICATION QUESTIONNAIRE 24 28 295

MILLARD COUNTY ARSENIC STUDY

WATER AND BEVERAGE CONSUMPTION QUESTIONNAIRE

Date _____ Name _____

Water Consumption

Considering all the sources of your drinking water (including home, work, school, etc.); please estimate how many 8 oz. glasses of plain water you drink in a typical 24 hour day (summer and winter) from each water source.

			Summer	Winter
1.	Hinckley public water supply	8 oz. glasses	_____	_____
2.	Delta public water supply	8 oz. glasses	_____	_____
3.	Private well at home	8 oz. glasses	_____	_____
4.	Private well other than at home	8 oz. glasses	_____	_____
	Location _____			
5.	Other water sources	8 oz. glasses	_____	_____
	Explain _____			

Beverages Consumed

Please estimate how many 8 oz. glasses of the following beverages you drink in a typical 24 hour day (summer and winter).

Beverages made with home tap water:			Summer	Winter
6.	Flavored drinks (Kool Aid, etc.)	8 oz. glasses	_____	_____
7.	Fruit Juice from Concentrate	8 oz. glasses	_____	_____
8.	Home canned juices	8 oz. glasses	_____	_____
9.	Postum, Pero, etc.	8 oz. glasses	_____	_____
10.	Coffee or Tea (made at home)	8 oz. glasses	_____	_____
11.	Other beverages with home tap water	8 oz. glasses	_____	_____
	Explain _____			

FIG. 4. Water and beverage consumption questionnaire.

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MILLARD COUNTY ARSENIC STUDY-WATER AND BEVERAGE CONSUMPTION QUESTIONNAIRE (Continued)

Beverages requiring no addition of tap water:		Summer	Winter
12. Carbonated Soft Drinks	8 oz. glasses	_____	_____
13. Non-Carbonated Soft Drinks	8 oz. glasses	_____	_____
14. Commercial Fruit & Vegetable Juices (V-8, Tomato Juice, Pineapple, etc.)	8 oz. glasses	_____	_____
15. Milk	8 oz. glasses	_____	_____
16. Beer	8 oz. glasses	_____	_____
17. Wine	8 oz. glasses	_____	_____
18. Coffee (from restaurant or other source away from home)	8 oz. glasses	_____	_____
19. Other beverages	8 oz. glasses	_____	_____

Explain _____

FIG. 4. Water and beverage consumption questionnaire (continued).

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times of day that one might consume water or beverages (such as morning upon rising, at noon for lunch, etc.). The questionnaire included places for summer and winter water consumption, community sources of water, various types of beverages including those made with home tap water and those not requiring addition of tap water.

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Consumption of arsenic from well water was estimated from participant responses to the "Water and Beverage Consumption Questionnaire." The participant's daily well water consumption estimates were tabulated separately for summer and winter. For the purposes of calculating an annual arsenic dose, the daily summer consumption estimate was applied to four months (126 days) while the daily winter consumption estimate was applied to eight months (239 days). The total estimated quantity of water consumed during a year (in liters) was then multiplied by the number of milligrams of arsenic per liter of the applicable well water, to derive the estimated annual dose of arsenic from well water (in milligrams). A crude estimated "Total Dose" was calculated also based on the annual dose times the number of years each participant had lived in the community.

ASSESSMENT OF HEALTH STATUS

Physical Examination Facility and Routine

Participants in the physical examination were given an appointment during the week of August 7, 1978. They were scheduled from 10 AM through 9 PM depending on their availability and work schedule.

The physical examinations were conducted in several rooms of the Delta High School. Typically as participants arrived they were received by study representatives who helped each of them fill out several forms including an informed consent form, a water and beverage consumption questionnaire, a health questionnaire, and a patient's personal history questionnaire. (See Figure 4 and Appendices A, B, and C.)

After completing the forms, the participants were taken to various stations for urine samples, hematocrit determinations, neurological examinations, and dermatological examinations. Upon completion of the physical examination, each participant's folder of examination papers was checked. The participant was then given a self-addressed, postage-paid envelope for a hair sample to be collected and mailed later.

DERMATOLOGICAL EXAMINATIONS

Dermatological examinations were carried out on 249 of the 250 individuals who came for physical examinations. Of the individuals examined, 43 (17.3%) were from Deseret; 101 (40.6%) were from Hinckley; and 105 (42.2%) were from Delta.

The examinations were carried out on a blind basis. The dermatologist had no knowledge of the community in which any individual resided. Body areas examined included face, back, abdomen, arms, legs, hands, and feet. No attempt was made to examine the chest, thigh, or genital areas unless questionable lesions were indicated by the study participants. Notations were made of

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the individual's eye and hair color as an indication of the susceptibility to actinic damage and skin cancer.

Participants were examined for specific signs of arsenic toxicity, including palmar and plantar (palms and soles) keratoses, diffuse palmar and plantar hyperkeratoses, and skin tumors in non-sun exposed areas. All such tumors were recorded except for obviously benign lesions such as seborrheic keratoses and warts. Any histologically-verified malignant tumors that were previously removed were noted. The location (i.e., sun-exposed vs palmar/plantar) and frequency of all keratoses and tumors were recorded. Any diffuse non-sun exposed hyperpigmentation was recorded, as were Mee's lines in nails. Arterial insufficiency was noted to assess any tendency toward "blackfoot disease" described for the Taiwan arsenic episode (Tseng, et al., 1968).

Following the dermatological examination, the previously completed "Health Questionnaire" (Appendix B) was reviewed by the dermatologist with the participant to clarify any positive responses and the relative frequency of viral or bacterial infections.

Neurological Examinations

All participants 47 years of age and younger were examined by the neurology team. Older participants were excluded because neuropathies incident to age were expected to be common. We focused on younger participants, in whom neuropathy was not generally expected, to see if an excess of neuropathy could be associated with high arsenic ingestion. In all, 150 participants received neurological examinations (Delta 67, Hinckley 53, and Deseret 30). Each participant filled out a "Patient's Personal History" prior to examination (see Appendix C for copy of forms used with neurological examinations).

All subjects were examined by a neurologist in a room separate from that used for electrodiagnostic tests. Light touch, pain, and temperature sensations were tested. An aesthesiometer (a modified Von Frey hair device) was used to measure thresholds to touch over the dorsum of fingers and toes. A 2 g force was taken as the lowest threshold for touch. A pinwheel was used over the feet and legs for detection of hypalgesia and sensory level. Cooled aluminum discs and wooden discs (1 cm^2) were used for evaluation of temperature sense in hands and feet. The number of correct responses in six trials was determined. Position sense was evaluated at the great toe. The number of correct responses out of ten were determined for 10° changes in position. Vibratory sense was evaluated by application of a 128 Hz tuning fork over the medial malleolus while the examiner palpated the lateral malleolus. Vibratory sense was rated as normal or decreased in comparison to that of the examiner. Deep tendon (stretch) reflexes were rated on an 0 to 4+ scale with 2 being normal, 1 just perceptible, 3+ unsustained clonus and 4+ sustained clonus. The general appearance of the hands and feet with respect to the degree of sweating, color, muscle mass, and skin temperature was also recorded.

Vital statistics for each subject, blood pressure (left arm, sitting position) and a systemic review using a standard National Board of Internal Medicine form were also obtained (see Appendix C). Participants were examined further if the medical history and neurological examination suggested the

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presence of involvement of the nervous system.

Electrodiagnostic studies were performed using a TE-4 electromyograph. All results were recorded on photographic paper for future reference. Median, ulnar and sural sensory nerves were studied in the right limbs.

Motor nerves were evaluated by applying a short duration (< 0.2 msec) supramaximal square wave pulse to a proximal and distal point on the nerve (above the elbow and at the wrist for median and ulnar nerves; at the knee and ankle for peroneal nerve) while recording from a small intrinsic hand or foot muscle. The time to first negative deflection of the evoked muscle action potential was recorded. Distal latency was subtracted from proximal latency and the difference divided into the distance between the two points of stimulation. Latencies, amplitude, and wave form measurements were recorded.

Sensory nerve conduction was evaluated by stimulating median and ulnar digital nerves while recording the nerve action potential at the wrist. The conduction distance was usually 13 cm. The sural nerve was stimulated at the lateral malleolus and recorded proximally 15 cm from the point of stimulation.

Temperatures were recorded by means of a skin (2 mm) thermistor using a Yellowsprings Telethermometer at the base of the first and fourth fingers and at the lateral malleolus.

Data were recorded on the reporting forms (Appendix C). Means and standard deviations for conduction velocities were then calculated for each nerve, geographic location, and age group.

Hematocrit Determinations

Blood was drawn by finger prick method. The first drop was discarded and the subsequent blood collected in a hematocrit tube. The tubes were centrifuged and the hematocrit readings made.

The criteria used to evaluate anemia was taken from the "Biology Data Book" (1974). The normal range for females 14 years of age and older is 37 to 47 percent and for males 40 to 54 percent. Single values were given for those under 14 years of age. People whose hematocrit readings were below the listed values or ranges were considered anemic.

Community Death Rates and Cancer Incidences

A retrospective epidemiological study was conducted to examine the possible association of arsenic consumption with cancer and vascular diseases in the West Millard County communities.

a. Cancer Incidence: Using Tumor Registry data, age adjusted cancer incidence rates were calculated for Millard County and several communities in Millard County. All types of cancers were included, including reported skin cancers. Skin cancer reporting depended on individual physicians since they were not required to report them. All forms of skin cancer could be included, not just the types associated with arsenic. Only seven percent of all cancers

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reported from Millard County were skin cancers.

The direct method of age adjustment was used. Age specific incidence rates for the standard population (Utah) were not readily available to enable use of the indirect method of age adjustment. An age adjusted incidence rate was also calculated for the residents of Millard County population. This was done for purposes of comparison to indicate whether county residents were included in community populations or otherwise.

b. Death Rates: Using vital statistic records of the State of Utah, age adjusted rates for cancer and three vascular diseases were calculated for 43 communities in Utah; including Hinckley, Delta, and Fillmore in Millard County. These rates were calculated to make a comparison for the death rates of the Millard County communities under study. All cancer-caused deaths were included in the study.

Since the study communities had small populations and age specific death rates for Utah were available, the indirect method of age adjustment was used in calculating death rates. An average of the 1960 and 1970 census data for 42 of the 43 cities was used to calculate death rates for the years 1956 through 1976. Since no 1960 census population breakdown data were available for Hinckley, the 1960 percentage of age distribution for Millard County was applied to the Hinckley population to estimate a 1960 age distribution for the residents of Hinckley. This estimate was averaged with the 1970 age distribution data and the resulting figures were used to calculate the age adjusted death rates for Hinckley.

In order to check the method for estimating Hinckley's 1960 age distribution, the 1970 age distribution was estimated by the same method. The 1970 estimate was compared to actual 1970 census data. The 1970 estimate had a larger population in the 65 year old and older age groups than the 1970 census data. If the same bias were introduced because of estimating the 1960 age distribution, the age adjusted death rates for Hinckley would be slightly lower than they should be.

STATISTICAL METHODS

Data collected in this study were summarized with various univariate, bivariate, and multivariate statistics. Data were keypunched on an Entrex 600/40 and a computer tape was generated and sent to the State of Utah's main frame computer, an Itel AS/5. This 4 megabyte computer operates under IBM/s MVS operating system software.

The data were analyzed using the statistical software package SAS, supplied by the SAS Institute, Raleigh, North Carolina. Also used was a program called ECTA based on a procedure by Leo Goodman, University of Chicago, Illinois.

The following procedures were used: 1) analysis of variance, 2) cluster analysis, 3) correlation analysis, 4) discriminant analysis, 5) factor analysis, 6) chi-square analysis of 2-way contingency tables, 7) log linear analysis of multi-way contingency tables, 8) regression analysis (least squares),

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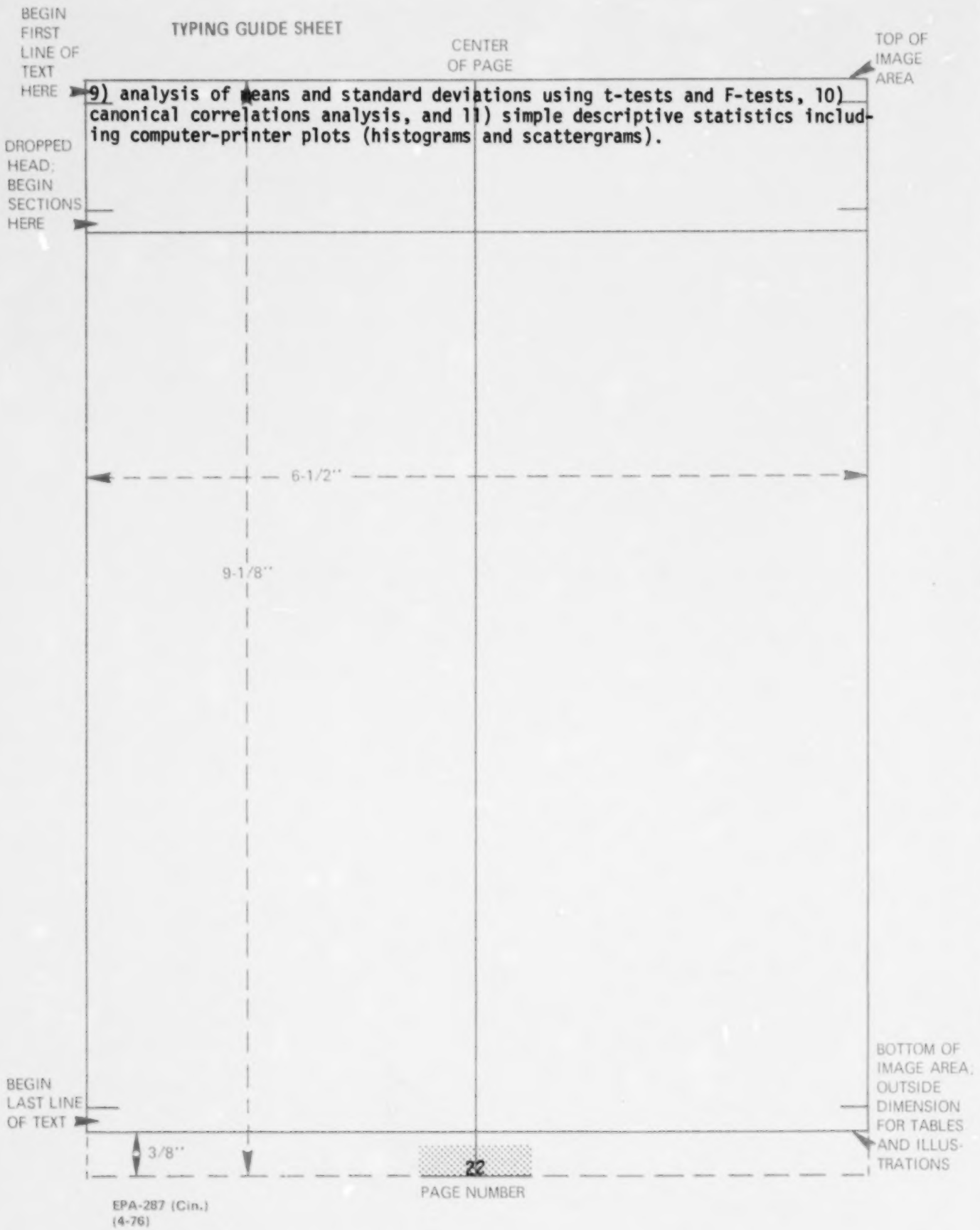
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9) analysis of means and standard deviations using t-tests and F-tests, 10) canonical correlations analysis, and 11) simple descriptive statistics including computer-printer plots (histograms and scattergrams).
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SECTION 3

RESULTS

ASSESSMENT OF EXPOSURE TO ENVIRONMENTAL ARSENIC

Arsenic in Drinking Water

Monthly water samples taken from Hinckley and Delta (May 1976-May 1977) showed arsenic concentrations averaging 0.180 mg/l for Hinckley and 0.019 mg/l for Delta (see Table 6).

6-1/2"

Table 6. Arsenic concentration in well water of three study communities.

Community	Number of samples	Arsenic content (mg/l) Mean	Range
Delta*	23	0.019	0.006 - 0.032
Hinckley**	12	0.180	0.150 - 0.220
Deseret***	27	0.210	0.053 - 0.750

9-1/8"

*Samples from Delta's three public wells sometimes individually and sometimes as mixed by distribution system.

**Samples from Hinckley's single public well.

***Single samples from 27 private wells in Deseret.

Deseret well waters averaged higher in arsenic content than did Hinckley's or Delta's. Families in Deseret whose wells tested less than 0.150 mg/l were not included in this study. Mean arsenic in well water of Deseret participants was 0.270 mg/l.

Arsenic in Ambient Air

Ambient air monitoring (July 1977-June 1978) showed an average of 0.005 $\mu g/M^3$ for arsenic (Range 0.001 to 0.015 $\mu g/M^3$). These figures are biased toward overestimating the amount of arsenic in ambient air because arsenic

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analyses were conducted only for the days with greater total suspended particulates in ambient air. Nonetheless, the amount of arsenic found was extremely low. We concluded that the amount of arsenic in the dry desert dust that became airborne particulates was not sufficient to materially bias interpretation of arsenic exposure via drinking water.

Arsenic Exposure Estimates

Water consumption data from participants in the physical examination was tabulated for each community (see Table 7). The consumption patterns were similar for each community. Individuals with similar work tended to have similar water consumption rates. Highest consumption of water was associated with farmers and others who worked out-of-doors in the area's hot (90°-105°F) desert environment. A few participants estimated their water consumption at more than eight liters per day in the summer.

Compared with "Daily Fluid Intake" as discussed in the National Interim Drinking Water Regulations, (Environmental Protection Agency, 1976), these participants reported higher than average fluid intake levels. This should not be unexpected given the area's desert environment.

Table 7. Daily summer water consumption rates for residents of three study communities.

9-1/8"

Community	Number of participants	Water consumption rate (liters/day) Mean	Range	Standard deviation
Delta	105	2.7	0.5 - 12.0	1.9
Hinckley	102	2.9	0.3 - 13.0	2.0
Deseret	43	2.4	0.3 - 8.0	1.4

Estimates of arsenic consumed by each study participant showed a wide range (see Table 8) within each community depending on the water consumption levels of each participant. Nonetheless, the mean arsenic consumption level was lowest in Delta (control) and highest in Deseret.

The product of length of time exposed and the estimated arsenic consumption rate was calculated as "Total Dose." Table 9 shows "Total Dose" estimates for Delta were substantially below those of Hinckley and Deseret, although some overlap was evident.

Arsenic in Hair

Initial sampling of school-age children and their parents in 1977 showed Hinckley residents averaged more arsenic in hair (0.82 µg/g) than in Delta residents (0.32 µg/g).

Sampling in 1978 as part of the physical examination showed a similar

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Table 8. Annual arsenic consumption from drinking water for study participants from three study communities.

Community	Number of participants	Arsenic consumption (mg) Mean	Range	Median
Delta (control)	105	24.2	4 - 135	17
"Exposed"	145	152.4	12 - 853	119
Hinckley	102	135.5	12 - 853	115
Deseret	43	192.5	14 - 736	148

Table 9. Estimated "total dose" of arsenic from drinking water for study participants from three study communities.

6-1/2"

Community	Number of participants	"Total arsenic dose" (mg) Mean	Range	Median
Delta (control)	105	716	32 - 8,052	443
"Exposed"	145	4,079	161 - 23,884	2,797
Hinckley	102	4,222	265 - 23,884	2,875
Deseret	43	3,743	161 - 14,250	2,419

9/8"

pattern. Table 10 shows Deseret residents to average somewhat less arsenic in hair than Hinckley residents but more than Delta residents. These arsenic in hair data were transformed to their logs and a Duncan's Multiple Range Test was performed. The results showed that Hinckley and Deseret did not differ from each other significantly but both were significantly different from Delta.

A "t"-test comparing Hinckley and Deseret (exposed) hair arsenic levels with Delta's (control) showed the difference to be statistically significant at $P = < 0.0001$.

When community of residence was ignored and hair arsenic levels were compared to estimated annual arsenic consumption, a dose-response relationship was clearly evident. Table 11 shows that those with the lower estimated annual doses, also had lower hair arsenic levels. The greater the annual dose of arsenic the higher was the arsenic level in hair, except in the over 300 mg of arsenic per year category, which was not significantly different from the other categories.

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Table 10. Comparison of arsenic in hair of residents of three communities.

Community	Number of samples	Arsenic concentration (µg/g) Arithmetic Mean	Range	Median
Delta (control)	68	0.32	0.10 - 3.10	0.20
"Exposed"	117	1.17	0.10 - 4.70	0.80
Hinckley	80	1.21	0.10 - 4.60	0.90
Deseret	37	1.09	0.10 - 4.70	0.65

Table 11. Arsenic level in hair compared to estimated annual arsenic dose.

6-1/2"
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N	Annual dose (mg)	Hair arsenic geometric mean (µg/g)	Grouping*
5	0 - 9	0.12	A
55	10 - 29	0.21	A
46	30 - 99	0.46	A
69	100 - 299	0.83	B
10	300+	0.47	AB

*Means with the same letter not significantly different at P = .01 (Duncan's Multiple Range Test).

Arsenic in Urine

Initial sampling of school-age children and their parents in 1977 showed Hinckley residents averaged more arsenic in their urine (0.098 mg/l) than did Delta residents (0.009 mg/l).

The 1978 physical examination sampling of urine showed a similar pattern, but with somewhat higher average concentrations. Part of the reason for the apparently higher concentrations compared to 1977 was the laboratory's manner of reporting of extremely low urinary arsenic levels. Part of the time the laboratory reported the lowest levels as "less than 0.010 mg/l," but subsequently reported the lowest levels as "less than 0.040 mg/l." In analysis of data these samples were handled as being 0.010 and 0.040 mg/l respectively.

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Table 12 shows Deseret to have the highest average arsenic-in-urine concentrations. These urinary arsenic data were transformed to logs and tested with the Duncan's Multiple Range Test. The results showed that as with hair arsenic, Hinckley and Deseret did not differ from each other significantly, but both were significantly different from Delta. A "t"-test showed the two exposed communities to have more arsenic in urine than Delta at the P = < 0.0001 level of significance.

Table 12. Comparison of arsenic in urine of residents of three communities.

Community	Number of samples	Arsenic concentration (mg/l) Arithmetic mean	Range	Median
Delta (control)	99	0.048	0.010 - 0.220	0.040
"Exposed"	135	0.185	0.025 - 0.660	0.158
Hinckley	95	0.175	0.025 - 0.580	0.150
Deseret	40	0.211	0.030 - 0.660	0.160

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Table 13 shows a strong dose-response relationship between estimated annual dose of arsenic and arsenic in urine. The higher the estimated arsenic dose per year, the higher the average level of arsenic found in urine samples.

Table 13. Arsenic levels in urine compared to estimated annual arsenic dose.

N	Annual dose (mg)	Urine arsenic geometric mean (mg/l)	Grouping*
10	0 - 9	.034	A
73	10 - 29	.044	A
63	30 - 99	.089	B
76	100 - 299	.152	C
12	300+	.302	D

*Means with the same letter not significantly different at P = 01 (Duncan's Multiple Range Test).

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ASSESSMENT OF HEALTH STATUS

Dermatological Findings

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Results of the dermatological examination are shown in Table 14. The finding of signs suggestive of arsenic toxicity was rare, with only 12 of 249 participants having any signs associated with arsenic ingestion. The fact that no participant had more than one sign (i.e. pigmentation and multiple cancers) suggests that the findings may have been incidental and not related to arsenic.

Table 14. Specific signs associated with arsenic ingestion as found in dermatological examinations.

Signs of arsenic ingestion	Control	Exposed
Palmar & plantar keratosis	1	2
Diffuse palmar or plantar hyperkeratosis	2	5
Tumors (nonsun-exposed)	0	0
Diffuse pigmentation (nonsun-exposed)	0	1
Arterial insufficiency	0	1
Mee's lines in nails	0	0
Total	3	9
Percent	2.86%	6.25%

6-1/2"

These twelve participants were not clustered among the more heavily exposed participants, as might be expected if high level arsenic exposure were responsible for the findings (see Table 15). For each indicator of exposure, the twelve tended to fall on either side of the mean for their respective community. The ages of the twelve averaged 57.5 years (range 26-82). Half of the twelve were females, half were males. The signs of arsenic ingestion given in Table 14, were regressed against annual arsenic dose and the log of annual dose, but no significant associations were found.

The "Health Questionnaire" (Appendix B) used by the dermatologist contained symptoms reported in the literature for populations exposed to high levels of arsenic. Table 16 displays the participants' responses. No meaningful differences were seen in the number of individuals experiencing symptoms associated with arsenic toxicity in the exposed communities compared to the control.

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Table 15. Four measures of arsenic exposure for the twelve participants who showed dermatological signs compatible with chronic arsenic poisoning.

Participant's community	Sign	Hair arsenic (µg/g)	Urinary arsenic (mg/l)	"Yearly Dose" (mg)	"Total Dose" (mg)	Age
Delta	Palmer & planter keratosis	0.1	0.025	20	1240	78
Delta	Diffuse palmer hyperkeratosis	0.6	0.070	135	6885	54
Delta	Diffuse palmer hyperkeratosis	0.4	0.050	12	240	59
Hinckley	Diffuse mild palmer hyperkeratosis	1.9	0.380	150	3900	26
Hinckley	Diffuse mild plantar hyperkeratosis	0.6	0.095	12	336	51
Hinckley	Diffuse palmer hyperkeratosis	3.0	0.420	117	7956	68
Hinckley	Diffuse pigmentation	0.1	0.130	79	4898	62
Hinckley	Arterial insufficiency	1.2	0.060	83	5700	82
Deseret	Palmer & plantar keratosis	0.2	0.180	61	4148	72
Deseret	Palmer & plantar keratosis	-	-	570	14250	73
Deseret	Diffuse plantar hyperkeratosis	0.4	0.160	604	7248	32
Deseret	Diffuse palmer hyperkeratosis	-	0.270	162	810	33

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Table 16. Symptoms recorded by study participants on a "Health Questionnaire" showing results from the study communities.

Symptoms	Control	Exposed
Fatigue and malaise	17.1%	11.1%
Arthritis	11.4%	9.0%
Sweating of hands & feet	6.7%	5.6%
Bacterial infection	3.8%	2.8%
Herpes simplex	9.5%	13.9%
Headache	15.2%	15.3%
Dizziness, trouble with balance	21.0%	13.9%
Cough or hoarseness	3.8%	6.9%
Paresthesia	2.9%	4.2%
Extended sun exposure	14.3%	13.2%
Any type of cancer	5.7%	7.6%
Abdominal pain or diarrhea	7.6%	6.3%

Neurological Findings

Nerve conduction data are presented in Table 17 according to age group, community, and nerve examined. The mean values for conduction velocity for any given nerve did not vary significantly with respect to age or community. However, some participants in each community and age group had below normal conduction velocities. For sensory nerves, velocities below 37 m/s were considered abnormal provided nerve temperature was above 30°C.

Sensory nerve conduction was observed to be primarily affected, with the sural nerve most often involved. Participants with low foot temperature explaining the slow conduction were also indicated. In such cases velocities were corrected according to the factor 1.8 m/s/degree. For example, a sural velocity of 32 m/s at 28°C could be corrected to 35.6 m/s at 30°C. The corrected velocity remains below normal. This is an estimated value which will vary somewhat from participant to participant because the nerve temperature

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Table 17. Nerve conduction velocity* values with respect to age, location and nerves examined.

Community/Age	Ulnar motor	Median motor	Ulnar sensory	Median sensory	Peroneal	Sural
Delta						
Ages 7-12	58 ± 11 (N= 2)	61 ± 4 (N= 8)	51 ± 3 (N= 8)	51 ± 6 (N= 8)	53 ± 4 (N= 8)	46 ± 4 (N= 8)
Ages 13-20	66 ± 9 (N= 9)	66 ± 10 (N=19)	50 ± 5 (N=18)	50 ± 4 (N=19)	53 ± 5 (N=19)	42 ± 3 (N=19)
Ages 21-30	65 ± 7 (N= 4)	62 ± 4 (N=10)	49 ± 4 (N= 7)	45 ± 4 (N=10)	51 ± 5 (N=10)	39 ± 3 (N=10)
Ages 31-40	63 ± 4 (N= 4)	63 ± 4 (N=21)	51 ± 5 (N=17)	47 ± 5 (N=21)	52 ± 4 (N=21)	43 ± 3 (N=20)
Ages 41-47	60 ± 9 (N= 4)	57 ± 6 (N= 9)	45 ± 7 (N= 8)	46 ± 8 (N= 9)	54 ± 6 (N= 9)	44 ± 4 (N= 8)
Hinckley						
Ages 7-12	67 ± 3 (N= 3)	59 ± 7 (N= 6)	52 ± 6 (N= 5)	48 ± 4 (N= 6)	55 ± 6 (N= 6)	45 ± 5 (N= 5)
Ages 13-20	65 ± 11 (N=10)	59 ± 7 (N=20)	47 ± 7 (N=16)	48 ± 7 (N=20)	54 ± 11 (N=20)	43 ± 4 (N=19)
Ages 21-30	67 ± 1 (N= 2)	64 ± 3 (N= 4)	46 ± 8 (N= 4)	50 ± 7 (N= 4)	52 ± 7 (N= 4)	42 ± 7 (N= 4)
Ages 31-40	62 ± 6 (N= 2)	63 ± 4 (N=13)	48 ± 5 (N=10)	46 ± 6 (N=13)	47 ± 6 (N=13)	42 ± 3 (N=13)
Ages 41-47	62 ± 2 (N= 3)	60 ± 4 (N= 9)	48 ± 7 (N= 5)	44 ± 7 (N= 9)	49 ± 7 (N= 8)	42 ± 6 (N= 8)
Deseret						
Ages 7-12	64 ± 8 (N= 8)	62 ± 8 (N=10)	46 ± 9 (N= 9)	47 ± 3 (N= 9)	58 ± 9 (N=10)	44 ± 3 (N=10)
Ages 13-20	52 ± 11 (N= 3)	63 ± 3 (N= 6)	50 ± 9 (N= 6)	47 ± 7 (N= 6)	50 ± 5 (N= 6)	43 ± 6 (N= 6)
Ages 21-30	67 ± 2 (N= 2)	67 ± 5 (N= 5)	46 ± 4 (N= 3)	48 ± 6 (N= 5)	58 ± 10 (N= 5)	43 ± 4 (N= 5)
Ages 31-40	67 ± 7 (N= 5)	57 ± 10 (N= 7)	49 ± 3 (N= 7)	47 ± 11 (N= 7)	53 ± 4 (N= 7)	41 ± 5 (N= 7)
Ages 41-47	(N= 0)	60 ± 1 (N= 2)	51 ± 8 (N= 2)	45 ± 2 (N= 2)	50 ± 3 (N= 2)	44 ± 4 (N= 2)

*All values in meters per second

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varies along its course depending upon the shape of the leg. Taking such participants into consideration, six exposed and six controls were found to have slowing of sural nerve conduction (Table 18). In Hinckley, five participants had other nerves with abnormal conduction, as did three in Deseret and two in Delta.

Table 18. Study participants judged to have abnormal nerve conduction (temperature corrected).

Community	Participant age range	Number of participants	Nerve with abnormal conduction
Delta (controls)	13-20	2	Sural
	21-30	3	Sural
	31-40	1	Sural
	31-40	1	Median Sensory
	41-47	1	Median and Ulnar Sensory
		8	(= 11.9% of 67 participants)
Hinckley	13-20	1	Ulnar Sensory
	13-20	1	Median and Ulnar Sensory
	21-30	1	Sural
	31-40	1	Sural
	31-40	1	Median Sensory
	31-40	1	Peroneal
	41-47	2	Sural
	41-47	1	Median Sensory & Peroneal
		9	(= 17.0% of 53 participants)
Deseret	7-12	1	Ulnar Sensory
	13-20	1	Sural
	31-40	1	Median Sensory
	31-40	1	Sural and Median Motor
		4	(= 13.3% of 30 participants)
Exposed (Hinckley and Deseret)		13	(= 15.7% of 83 participants)

The data can be viewed from the standpoint of number of nerves with abnormal conduction. More nerves were involved in exposed participants; median motor and peroneal nerves in addition to the median sensory, ulnar sensory, and sural which were also seen in control participants (Table 19).

Participants with nerve conduction slowing were found in all three communities. The number of participants involved was small but the data

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indicate a slightly increased proportion of participants with slowing of nerve conduction among the exposed participants. Actual nerve conduction velocities were regressed against annual arsenic dose and the log of annual dose, but no significant associations were found.

Table 19. Abnormal nerve conduction velocities (temperature corrected) by community and age of participants according to nerves examined.

Community	Age range	Nerves with abnormal conduction: Sural	Median motor	Median sensory	Ulnar sensory	Peroneal
Delta	7-12	0	0	0	0	0
	13-20	2*	0	0	0	0
	21-30	3	0	0	0	0
	31-40	1	0	1	0	0
	41-47	0	0	1	1	0
Total Delta (control)		6/65=9.2%	0%	2/67=3.0%	1/58=1.7%	0%
Hinckley	7-12	0	0	0	0	0
	13-20	0	0	1	2	0
	21-30	1*	0	0	0	0
	31-40	1	0	1	0	1
	41-47	2	0	1	0	1
Total Hinckley		4/49=8.2%	0%	3/52=5.8%	2/40=5.0%	2/51=3.9%
Deseret	7-12	0	0	0	1	0
	13-20	1	0	0	0	0
	21-30	0	0	0	0	0
	31-40	1	1	1	0	0
	41-47	0	0	0	0	0
Total Deseret		2/30=6.7%	1/30=3.3%	1/29=3.4%	1/27=3.7%	0%
Total Exposed (Hinckley and Deseret)		6/79=7.6%	1/82=1.2%	4/81=4.9%	3/67=4.5%	2/81=2.5%

*One with nerve temperature less than 30°C.

Neurological and physical findings are summarized in Table 20. No trends were noted for any particular neurological finding or geographical location. In general, typical signs and symptoms of arsenic intoxication were not present in any of the participants examined, but slight impairment of sensation

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in the feet was found in two participants of each community.

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Table 20. Neurological and physical findings.

Findings	Community		
	Delta	Hinckley	Deseret
Cold feet	3	2	0
Cramps	8	6	2
Sweating	0	4	2
Decreased reflexes	3	0	0
Decreased sensation	2	2	2
Carpal tunnel syndrome	0	0	1

Hematocrit Findings

Table 21 shows results of hematocrit testing. The percentage of participants with anemia tended to be higher in the exposed communities; however, two of the four anemics in Deseret came from one family (mother and son, age 7). Another son of the same family (who at 2 years old, was too young for this study) was subsequently found to have anemia also. Two other sons (ages 14 and 9) were study participants, but did not show anemia.

Table 21. Anemia in study participants from three study communities.

Community	Number tested	Anemia	
		Number	Percent
Control (Delta)	100	5	5.0
Exposed	137	10	7.3
Hinckley	95	6	6.3
Deseret	42	4	9.5

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If a familial tendency toward anemia existed in this Deseret family, the

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percentage of anemia for Deseret could be somewhat biased toward the high side. No other familial anemias were observed.

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Because of the apparent trend toward more anemia in communities with increasingly high arsenic levels in drinking water, a chi square test for a linear trend was made (Brown and Benedetti, 1979). No significant trend was found (P= .33).

Table 22 shows that Hinckley participants with anemia were significantly older than anemic participants from Delta or especially from Deseret. Only in Hinckley were the majority of anemics female. Hair and urine arsenic was greater among anemic participants from the exposed communities as was estimated annual arsenic dose.

Table 22. Characteristics of anemic participants from three communities.

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9-1/8"

Characteristic		Delta	Hinckley	Deseret
Age:	Mean	26.4	56.0	16.3
	Range	8 - 46	30 - 82	7 - 35
Sex:	% Female	40	67	25
Hair arsenic:	Mean	0.15	0.62	1.65
(µg/g)	Range	0.1-0.2	0.1-1.2	0.4-2.6
Urine arsenic:	Mean	0.044	0.099	0.188
(mg/l)	Range	0.025-0.065	0.050-0.150	0.030-0.530
Estimated annual dose of arsenic:	Mean	16.8	103.0	78.5
(mg/year)	Range	4 - 49	12 - 218	23 - 153

Cancer Incidence

Age adjusted cancer incidence rates for Millard County are shown in Figure 5. These rates (derived from tumor registry data using the direct method of age adjustment) show Hinckley to have a somewhat lower incidence

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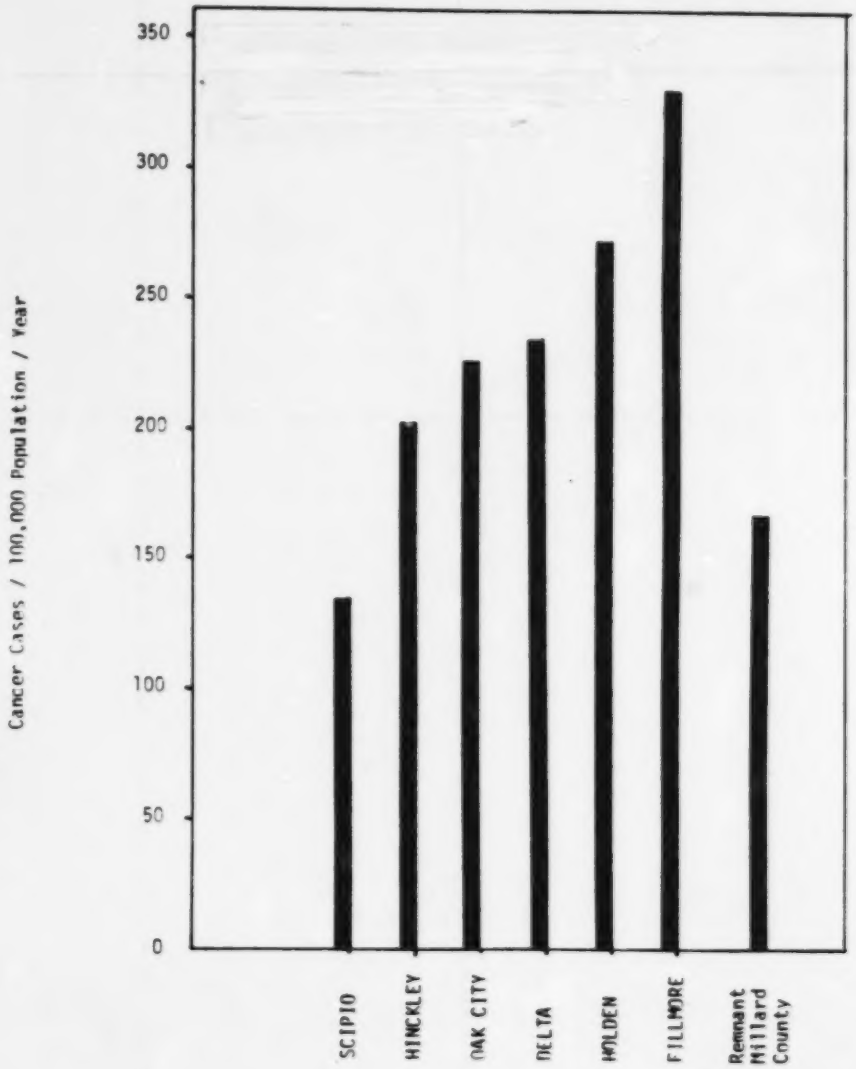

FIG. 5. Age adjusted cancer incidence for communities of Millard County, Utah, 1966-1976 (direct method of age adjustment).

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of cancer (1966-1976) than did Delta. The highest incidence was found for Fillmore, the Millard County seat (population 1,411).

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Community Death Rates

Table 23 shows age adjusted death rates (indirect adjustment method) for cancer, cerebrovascular, cardiovascular, and arteriosclerosis for 43 Utah communities for the years 1956-1976. Figures 6 - 9 show graphically the relationship of the various community death rates to each other.

Cancer--Compared to 42 other Utah communities (see Figure 6), Hinckley had the highest cancer death rate (138 per 100,000). Delta's cancer death rate was among the higher of these Utah communities. The Hinckley cancer deaths were of specific interest because of the community's arsenic exposure. For the 21 years (1956-1976) for which the rate was calculated, 14 cancer deaths were reported for Hinckley. The types of cancer were the same types most frequently reported for Utah: lung, breast, large intestine, prostate, stomach, leukemia, kidney, uterus, bone, and connective tissue. There was no unusual cancer death pattern established for the arsenic exposed community.

6-1/2"

Additional insight on cancer rates in Hinckley can be obtained by noting the age specific death rates for Hinckley compared to other Millard County communities (Table 24). Hinckley cancer deaths were limited to the older age categories (over 45 years); whereas, cancer deaths in people under 45 were observed in Delta and Fillmore, and the State of Utah as a whole.

Circulatory Diseases--Figures 7 and 8 show Hinckley had lower age adjusted death rates for cerebrovascular and cardiovascular diseases, than Delta had. Figure 9 shows Hinckley's death rate for arteriosclerosis to be higher than Delta's.

Age specific death rates for these three circulatory diseases (Table 24) show that deaths occurred in the older age categories for the study communities. For Hinckley, all cerebrovascular diseases occurred in individuals over 70 years of age. Hinckley cardiovascular disease deaths were more common in the 70 - 74 year age span.

Statistical Analyses

For statistical treatment of the data, Hinckley and Deseret participants were combined since they constituted the "exposed" participants while Delta participants functioned as "controls."

"t"-Test--A simple "t"-test (Goodnight, 1979*c*) was performed to compare average health and exposure indicators from the control and exposed communities. Table 25 shows that only the exposure indicators were significantly different between exposed and control communities. None of the health indicators were significantly different between exposed and control communities.

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Chi Square Test--For those health indicators for which incidence could be calculated, a χ^2 test (Sall, 1979*b*) was performed to test the null hypothesis that the incidence in each community was the same. Table 26

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Table 23. Age adjusted death rates (per 100,000) for four diseases for selected Utah Communities, 1956-1975 (indirect method of age adjustment).

COUNTY	CITY	CODE	CANCER	CEREBRO-VASCULAR	CARDIO-VASCULAR	ARTERIO-SCLEROSIS
BEAVER		01				
	BEAVER	01	135	123	274	38
	MILFORD	02	123	70	263	25
BOX ELDER		02				
	BRIGHAM CITY	01	80	73	176	21
	TREMONTON	02	85	36	194	16
	GARLAND	04	106	80	171	7
CACHE		03				
	LOGAN	01	73	75	153	12
	SMITHFIELD	02	95	79	173	19
	HYRUM	10	87	46	171	11
	WELLSVILLE	11	116	76	205	9
CARBON		04				
	DRAGERTON	01	91	39	138	10
	HELPER	02	122	32	258	9
	PRICE	03	124	58	233	10
	WELLINGTON	05	70	69	206	11
DAVIS		06				
	BOUNTIFUL	01	105	63	217	14
	CLEARFIELD	03	95	127	157	6
	LAYTON	06	99	55	223	27
GRAND		10				
	MOAB	01	129	73	214	14
IRON		11				
	CEDAR CITY	01	95	68	200	2
	PARAWAN	04	71	45	254	14
JUAB		12				
	NEPHI	01	61	81	196	41
	EUREKA	02	130	95	295	24
MILLARD		14				
	DELTA	01	116	82	170	22
	FILLMORE	02	90	82	177	24
	HINCKLEY	03	138	54	138	36
SAN JUAN		19				
	BLANDING	01	106	68	134	8
	MONTICELLO	02	64	55	119	37
SANPETE		20				
	EPHRAIM	01	95	76	218	10
	MANTI	02	83	81	187	8
	GUNNISON	04	109	46	257	16
	MT. PLEASANT	07	84	73	236	17
TOOELE		23				
	GRANTSVILLE	01	116	48	329	9
	TOOELE	02	119	50	251	9
UTAH		25				
	AMERICAN FORK	01	114	87	187	13
	LEHI	02	104	76	216	15
	PAYSON	04	113	76	216	28
	PLEASANT GROVE	05	73	79	185	26
	PROVO	06	54	50	141	11
	SPANISH FORK	07	105	80	224	14
	SPRINGVILLE	08	98	78	196	18
WASATCH		26				
	HEBER	01	80	79	279	14
WASHINGTON		27				
	ST. GEORGE	01	75	49	173	17
	ENTERPRISE	03	66	69	115	6
	HURRICANE	04	69	84	210	10

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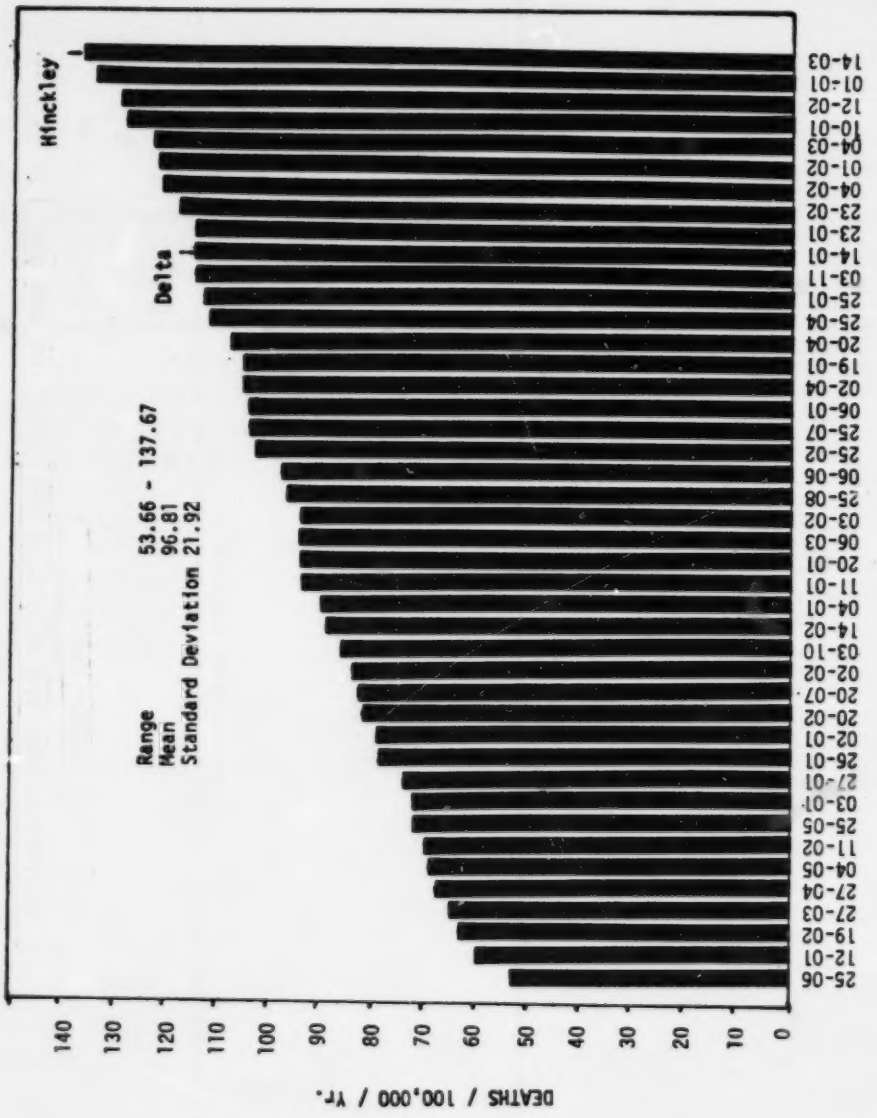

FIG. 6. Age adjusted cancer death rates in selected Utah cities, 1956 - 1975.

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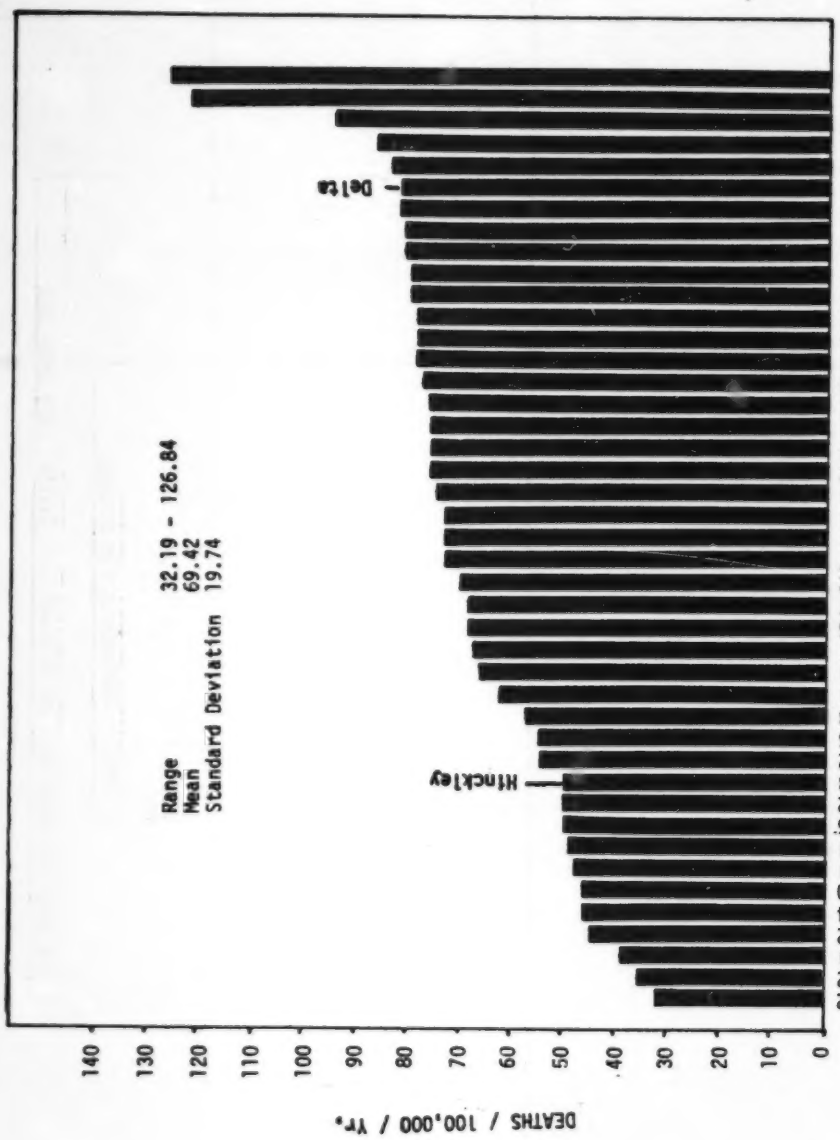

FIG. 7. Age adjusted cerebrovascular death rates in selected Utah cities, 1956 - 1975.

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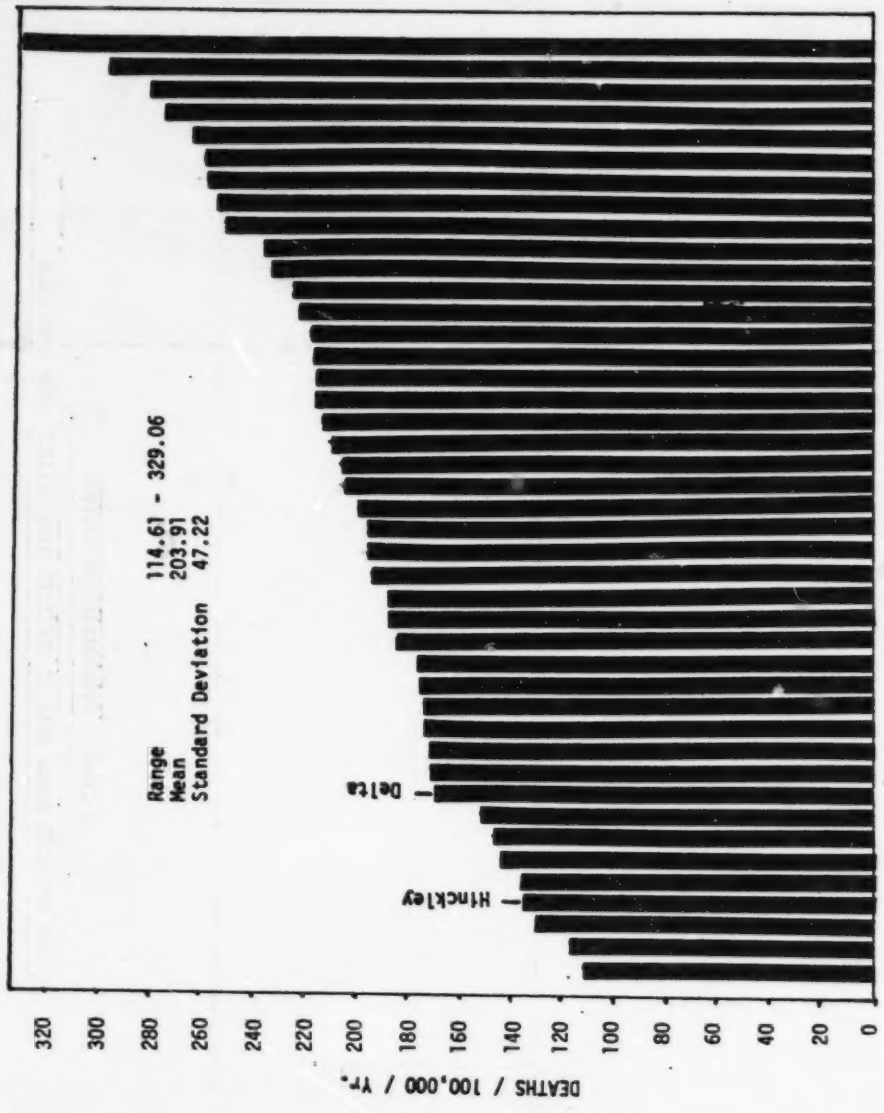

FIG. 8. Age adjusted cardiovascular death rates in selected Utah cities, 1956 - 1975.

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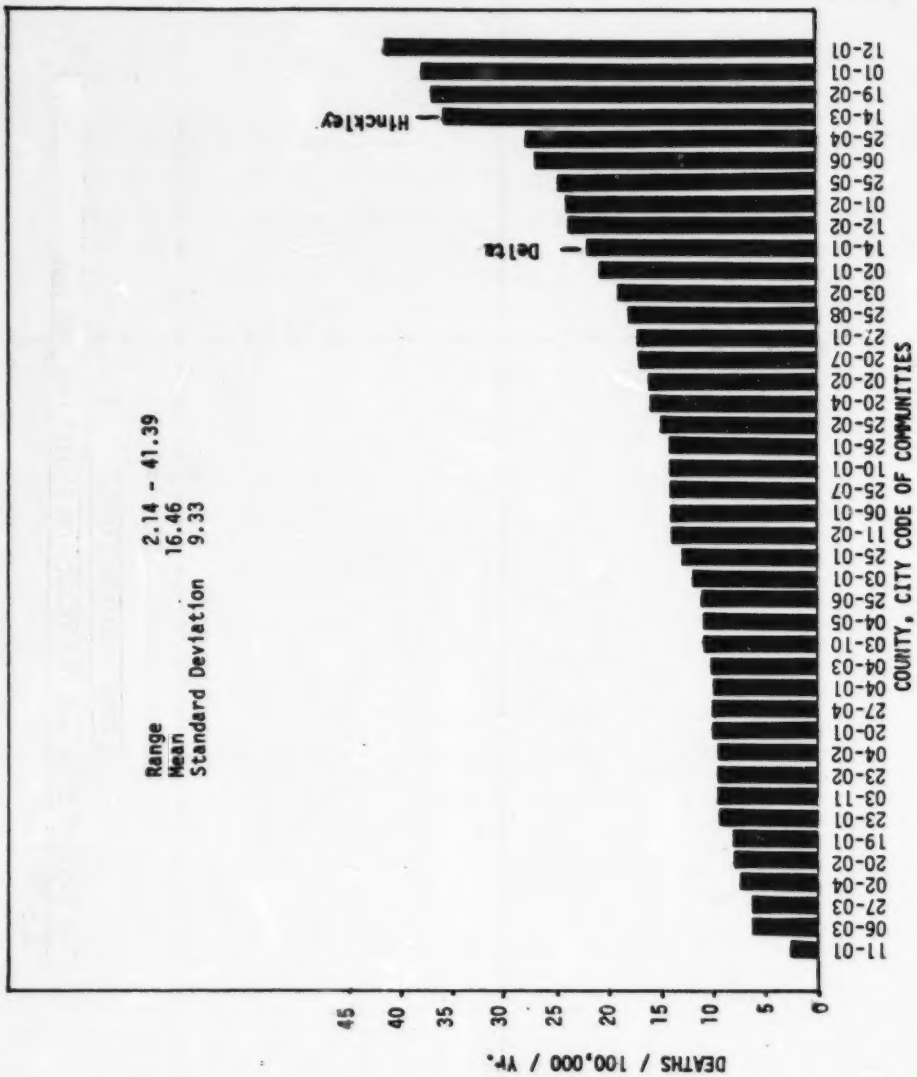

FIG. 9. Age adjusted arteriosclerosis death rates in selected Utah cities, 1956 - 1975.

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Table 24. Age specific death rates (deaths/100,000/year) for Utah and three Millard County communities, 1956 thru 1975 for cancer, cardiovascular disease, cerebrovascular disease, and arteriosclerosis, showing numbers of deaths and the average size of the age groups.

Community Characteristics	Age Groups and (Number of Deaths)					
	0-4	5-14	15-24	25-44	45-64	65+
CANCER						
State	7 (158)	6 (274)	6 (223)	19 (875)	149 (4749)	558 (7680)
Fillmore	0	14 (1)	0	17 (1)	196 (13)	706 (25)
Delta	0	0	22 (1)	61 (4)	189 (11)	986 (29)
Hinckley	0	0	0	0	390 (6)	1053 (8)
CARDIOVASCULAR						
State	1 (25)	0.4 (18)	1 (34)	18 (840)	275 (8788)	2079 (28587)
Fillmore	0	0	0	17 (1)	392 (26)	1638 (58)
Delta	0	0	0	30 (2)	344 (20)	1599 (47)
Hinckley	0	0	0	0	325 (5)	1316 (10)
CEREBROVASCULAR						
State	1 (24)	0.5 (23)	1 (36)	4 (201)	52 (1651)	797 (10965)
Fillmore	0	0	0	0	60 (4)	1017 (36)
Delta	0	0	0	0	34 (2)	1088 (32)
Hinckley	0	0	0	0	0	789 (6)
ARTERIOSCLEROSIS						
State	0	0.07 (3)	0.2 (7)	0.5 (21)	13 (406)	202 (2781)
Fillmore	0	0	0	0	15 (1)	311 (11)
Delta	0	0	0	0	17 (1)	272 (8)
Hinckley	0	0	0	0	65 (1)	395 (3)
AGE GROUP SIZE						
State	119,004	224,417	175,607	227,502	159,613	68,759
Fillmore	157	347	202	293	332	177
Delta	202	400	224	330	291	147
Hinckley	40	108	57	79	77	38

shows the variables considered and that the health indicator incidences did not differ significantly between exposed and control communities, thus we were unable to reject the null hypothesis.

Factor Analysis -- Twenty-nine selected health and exposure indicators were subjected to a factor analysis (Sall, 1979a). Pearson product-moment correlation co-efficients were used. Five of the indicators were transferred to their natural logs because of their non-normal distribution, to make them more "normal." Table 27 shows the 29 indicators.

Figure 10 shows 11 factors developed by the factor analysis (using "Equamax" rotation method). The factors are ranked in order of the amount of variability explained with the basic information they contain. Variables within each factor are ranked in order of the variable's importance to the

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Table 25. A group analysis comparison of means for health and exposure indicators in exposed and control communities.

Variable	t Test sig. level	Control number	Control mean & std. dev.	Exposed mean & std. dev.	Exposed number
Urine arsenic	P <.0001*	99	48.1±30.7	185.3±124.3**	135
Annual dose	P <.0001*	105	24.2±22.1	152.4±130.8**	145
Total dose	P <.0001*	105	716 ±1112	4079 ±3807**	145
Hair arsenic	P <.0001*	68	.32±.49	1.17 ±1.09**	117
Urine/hair ratio	N.S. (.45)*	66	269±219	448 ±581**	111
Age	N.S. (.46)	105	38.7±19.3	40.6 ±21.5	145
Years in community	N.S. (.40)	105	26.2±15.4	28.0 ±17.6	145
Ulnar motor d.l.***	N.S. (.04)	24	2.29±0.31	2.53 ±0.59**	38
Ulnar motor v.****	N.S. (.88)	23	63.8±8.2	64.1 ±8.5	38
Median motor d.l.	N.S. (.43)	67	2.98±0.46	3.05 ±0.55	82
Median motor v.	N.S. (.13)	67	62.6±6.8	61.0 ±6.5	82
Ulnar sensory d.l.	N.S. (.18)	58	2.63±0.33	2.73±0.45	67
Ulnar sensory v.	N.S. (.06)	58	50.2±5.3	48.1±6.6	67
Median sensory v.	N.S. (.30)	67	47.8±5.4	46.8±6.4	81
Peroneal d.l.	N.S. (.88)	67	3.99±0.90	3.97±0.92	81
Peroneal v.	N.S. (.68)	67	52.3±4.6	52.7±8.4**	81
Sural v.	N.S. (.77)	65	42.5±3.8	42.7±4.4	79
Hematocrit	N.S. (.48)	100	43.5±3.6	43.2±3.6	137

* These t-test significance levels were computed using log-transformed data due to non-normality of the variable.

** Indicates the standard deviation is significantly different between groups by 1% or less, using untransformed data.

*** d.l. = Distal latency for nerve.

**** v. = Velocity for nerve conduction.

factor.

The factor that explained the most variability in the data set, "Factor 1," could be called the "exposure factor" as expressed by the interrelationships of estimated annual and total doses of arsenic, by living in exposed or control communities and by the amount of arsenic found in hair and urine samples. The significant correlations among these exposure variables takes on added importance since none of the health indicators correlated with this exposure factor.

"Factor 2" could be called the "age factor" since years in community are related to age.

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Table 26. Chi square test comparing incidence of symptoms in exposed and control communities.

Variable	Chi square sig. level	Control percent	Control no.	Exposed percent	Exposed no.
Abnormal Dermatology	N.S. (P=.22)	2.9%	3	6.3%	9
Palmer/Plantar Keratosis	N.S. (P=.76)	1.0%	1	1.4%	2
Diffuse Palmer/Plantar Hyperkeratosis	N.S. (P=.46)	1.9%	2	3.5%	5
Any type Cancer	N.S. (P=.61)	4.8%	5	3.5%	5
Numbness & Tingling	N.S. (P=.80)	11.4%	12	10.4%	15
Touch & Temperature Sense	N.S. (P=.13)	1.0%	1	4.2%	6
Reduced Energy	N.S. (P=.70)	10.5%	11	9.0%	13
Nerve Conduction Slowing	N.S. (P=.51)	11.9%	8	15.7%	13
Anemia	N.S. (P=.47)	5.0%	5	7.3%	10
Sex = Female	N.S. (P=.82)	55.2%	58	53.8%	78

"Factor 3" primarily contained a sex/arsenic-in-hair relationship. Women tended to have less arsenic in their hair than men.

"Factor 4" was a composite factor showing a relationship between sex, reduced energy level, and some neurological measurements. This factor indicated women reported more "reduced energy levels" than men. Women had higher median sensory, nerve velocity and lower distal latency for the median motor nerve.

"Factor 5" encompassed correlations between neurological measurements as did "Factor 10."

"Factor 6" contained the relationship between sural nerve velocity and designation of nerve slowing. It indicated that the lower the sural nerve velocity became, the more likely the neurologist was to judge the individual

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Table 27. Health and arsenic exposure indicators used in factor analysis.

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Test	Indicator	Units
General	Age	years
	Sex	male/female
Exposure	Urine arsenic*	mg/liter
	Hair arsenic*	µg/gram
	Annual dose*	milligrams
	Years in community	years
	Total dose*	milligrams
	Urine/hair ratio*	ratio
	Community	exposed/control
Dermatologic exam	Arterial insufficiency	yes/no
	Palmer/plantar keratosis	yes/no
	Diffuse palmer/plantar hyperkeratosis	yes/no
	Hyperpigmentation	yes/no
Questionnaire	Any type cancer	yes/no
	Numbness & tingling	yes/no
	Reduced touch & temperature sense	yes/no
	Reduced energy level	yes/no
Neurological exam	Ulnar motor distal latency	seconds
	Ulnar motor velocity	meters/second
	Median motor distal latency	seconds
	Median motor velocity	meters/second
	Ulnar sensory velocity	meters/second
	Median sensory velocity	meters/second
	Peroneal distal latency	seconds
	Peroneal velocity	meters/second
	Sural velocity	meters/second
	Nerve slowing	yes/no
Hematocrit	Hematocrit	%
	Anemia	yes/no

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* Transformed to natural log.

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Factor 1	Factor 2	Factor 3
1. Annual dose	Years in community	Urine/hair ratio
2. Community	Age	Hair arsenic
3. Urine arsenic		Sex
4. Total dose		
5. Hair arsenic		

Factor 4	Factor 5	Factor 6
1. Median sensory velocity	Peroneal distal latency	Sural velocity
2. Median motor distal latency	Ulnar sensory velocity	Nerve slowing
3. Reduced energy level	Peroneal velocity	
4. Sex		

Factor 7	Factor 8	Factor 9
1. Anemia	Arterial insufficiency	
2. Hematocrit	Reduced touch & temp. sense	Diffuse palmer/ planter hyper-keratosis
3. Hyperpigmentation		Any type cancer

Factor 10	Factor 11
1. Ulnar motor velocity	Numbness & tingling
2. Median motor velocity	

Figure 10. Factors developed by factor analysis ("Equamax" rotation).

as having nerve slowing. Half of the nerve slowing observed was associated with the sural nerve.

"Factor 7" contained hematocrit, anemia, and hyperpigmentation variables. The relationship between anemia and hyperpigmentation resulted from the fact that the only person in the study with hyperpigmentation also had anemia.

"Factor 8" and "Factor 11" dealt with abnormalities of the extremities.

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"Factor 8" implied that if the dermatologist saw arterial insufficiency in the extremities, the participant was more likely to have claimed to have had "reduced sense of touch or temperature sensations in feet or hands." "Factor 11" simply represented participant claims to have had persistent or unusual numbness, tingling or sensations of 'pins and needles' in feet or hands.

The relationship in "Factor 9" indicated that if the dermatologist found diffuse palmer/plantar hyperkeratoses, the participant was more likely to have answered "yes" to the question, "have you ever had any type cancer?"

All of the relationships seen in Factors 2 through 11 could occur in any community of people without arsenic exposure. Indeed this factor analysis indicated arsenic exposure was independent of these health indicators.

Discriminant Analysis

For discriminant analysis, the classification criterion was determined by a general square distance measure (Goodnight, 1979*b*). Two groups were considered: the arsenic exposed participants (Hinckley and Deseret residents) and control participants (Delta residents). Health problems upon which the discrimination was based were: Nerve conduction slowing as determined by the neurologist (see Table 18), dermatological signs compatible with chronic arsenic poisoning as determined by the dermatologist (see Table 15), and anemia (see Tables 21 and 22). When there were missing values, observations were deleted. This meant that only participants under age 48, who received the neurological examinations, were considered in this analysis. There were 141 observations, 79 exposed and 62 controls.

The discriminant analysis misclassified 49.6% of the participants. Of the 79 exposed participants only 15 (19.0%) were classified as exposed based on the health indicators. Of the 62 control participants, 6 (9.7%) were misclassified as exposed.

Since almost half (70/141) of the participants were misclassified by the discriminant analysis, the analysis implies that the health problems were not sufficiently related to arsenic exposure in this study population to permit discrimination (differentiation) between exposed and control participants.

Canonical Correlation Analysis

In order to avoid any bias from using community-of-residence as the definition of exposure to arsenic, a canonical correlation (Goodnight, 1979*a*) was performed without using community-of-residence data. As in the discriminant analysis, nerve conduction slowing, arsenic-like dermatological signs and anemia were used as the set of health-problem-indicating (dependent) variables. Arsenic levels in hair and urine, estimated annual arsenic dose, years-in-community, and sex were used as the set of explanatory (independent) variables.

No significant canonical correlation was found, indicating no evidence of a relationship between health problems and arsenic exposure.

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SECTION 4

DISCUSSION AND CONCLUSIONS

This study had a relatively small study population, but compensating for small size (from a statistical standpoint) was the fact that we were dealing with a homogenous, stable population with minimum influence from cigarette smoking due to the predominantly "Mormon" life-style. We had a distinct portion of the study population with a significantly higher exposure to arsenic from drinking water. The study results showed consistency and logic within themselves. For example, in the factor analysis, the data were sufficient to develop several internally consistent factors that gave confidence in the descriptive ability of the data set.

This study showed a clear relationship between the amount of arsenic consumed in drinking water and the amount of arsenic in scalp hair (n=185, r=.47, P=<.0001) and urine (n=234, r=.70, P=<.0001). This relationship was expected since the ingestion of an element obviously will result in its excretion. Arsenic levels found in hair and urine samples were simply considered tools to evaluate arsenic exposure.

Our study population was not as heavily exposed to arsenic as were populations described by Tseng et al. (1968) in Taiwan or by Borgono and Greiber (1972) in Chile. Likewise, the signs and symptoms they ascribed to arsenic exposure from drinking water were not duplicated in these Utah communities.

If there was a common theme in arsenic exposure episodes in the literature, it was the presence of cutaneous hyperkeratotic lesions and hyperpigmentation. The literature led us to believe that even at these relatively lower arsenic-in-water levels we could expect an excess of cutaneous manifestations of arsenic toxicity, but we did not find any excess. Benign skin lesions, that the National Academy of Science (1977) regarded as "sensitive indexes of exposure," were not found to correlate with actual arsenic exposure data. The few observed dermatological signs were scattered singly among individuals of the whole study population, rather than occurring together on individuals with higher arsenic exposure.

Anemia was found, but not significantly more often among exposed participants. Nerve conduction slowing was found in participants of each study community but was not correlated with arsenic exposure. Typical signs and symptoms of arsenic intoxication were not found in any of the study participants.

Cancer incidence and death rates did not suggest an excess of cancer in the exposed community. In fact the data implied that cancer incidence was relatively low in Hinckley. Deaths due to cancer in Hinckley were absent in

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younger age groups and most common in people over 70 years of age. Indeed people seemed to live to "ripe-old" ages in these study communities.

Our hypothesis that arsenic consumption at the levels found in Hinckley and Deseret drinking water would result in signs and symptoms of chronic arsenic poisoning, was not confirmed by this study. Residents of Hinckley and Deseret appeared to be as healthy as Delta residents. When community of residence was ignored and health indicators were compared with measures of arsenic exposure, the participants with higher arsenic exposure did not show evidence of health problems any more than did participants with lower arsenic exposure.

After reviewing these data compared to published data, we wondered why the various episodes ascribed to arsenic exposure differed so much in signs and symptoms of illness. Assuming arsenic was an indisputable exposure factor in these episodes, what confidence do we have that some other toxic exposure factor may not have also been present to produce some of the signs and symptoms unique to the various episodes? For example, why "blackfoot disease" in Taiwan but not in Chile? Why were children the predominant patients in Chile? Is it possible that factors such as dietary habits or malnutrition might influence the expression of various signs and symptoms of arsenic intoxication?

One aspect of these arsenic episodes that has not been adequately assessed is the species of arsenic present in the implicated waters. Since As^{+3} is known to be much more toxic than As^{+5}, the species of arsenic in water may explain why Hinckley water may not produce toxicity, while arsenic in water elsewhere might. The species of arsenic in Hinckley water was determined to be predominantly (86%) As^{+5} by Dr. Kurt Irgolic of Texas A & M University, College Station, Texas (Personal communication, 13 February 1980).

The present drinking water standards, promulgated in the National Interim Primary Drinking Water Regulations, has a "Maximum Contaminant Level" of 0.05 mg/l for arsenic. This standard is based on the assumption that at an average water intake of two liters per day, arsenic intake from water would not exceed 100 µg per day (36.5 mg/year).

In this study, no adverse health effects were found for exposed people consuming an average of more than 150 mg of arsenic from well water per year. This indicates the amount of arsenic consumed from water by the exposed population of this study was four times (150/36.5 = 4.1) the maximum allowed by the current standard without evidence of adverse health effects.

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APPENDIX A

MILLARD COUNTY ARSENIC STUDY

RELEASE

I do hereby authorize information obtained through physical examinations and special clinical studies to be released to the Millard County Arsenic Study conducted by the Bureau of Environmental Epidemiology of the Utah State Division of Health. I understand that information accumulated by this study will not be used in any way which endangers my right to privacy.

I also request that any important health problems discovered through my medical examination be brought to the attention of my family physician.

_____M.D.
Physician's Name

_____
Physician's Address

Signed_____

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APPENDIX B

24 28 296

MILLARD COUNTY ARSENIC STUDY
HEALTH QUESTIONNAIRE

Date _____ Number _____

Have you recently had . . .	Yes	No
1. Any unusual weight loss.	○	○
2. Trouble with your energy level that has made your daily activities harder.	○	○
3. Any swelling of the joints, or swelling or redness of the hands or feet.	○	○
4. Darkening of certain skin areas.	○	○
5. Thickening of skin areas, either scaly masses or warty forms.	○	○
6. Persistent or unusual numbness, tingling, or sensations of "pins and needles" in feet or hands.	○	○
7. Excessive sweating of the hands and feet.	○	○
8. Discoloration of urine.	○	○
9. Episodes of fainting, sores in the mouth, and awareness of increased salivation.	○	○
10. Any unusual coldness or discoloration of fingers or toes.	○	○
Have you ever had . . .		
11. History of anemia.	○	○
12. Any unusual colicky abdominal pain, vomiting or diarrhea.	○	○
13. Frequent boils or other skin infections.	○	○
14. Any frequent cold sores or fever blisters.	○	○
15. Severe or frequent headaches.	○	○
16. Feelings of dizziness or trouble with your balance.	○	○
17. Any unexplained cough or hoarseness.	○	○
18. Reduced sense of touch or temperature sensations in your feet or hands.	○	○
19. Extended exposure to the sun either through sun bathing or working in the sun without your shirt (4 hours a day for 4 months out of the year).	○	○
20. Any type of cancer.	○	○
21. Substantial exposure to pesticides. List most heavily used; including any arsenical pesticides: _____ _____	○	○

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APPENDIX B-1

24 28 297

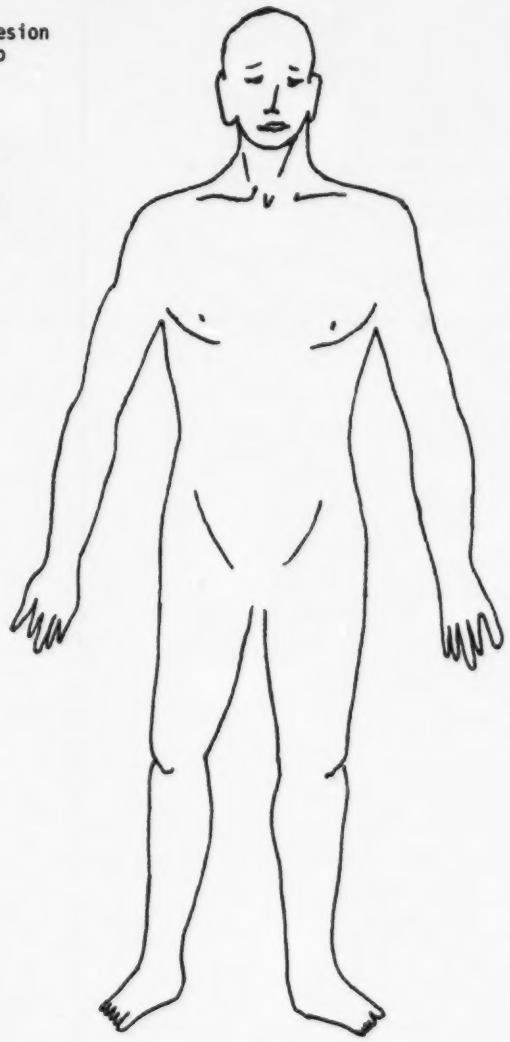
DERMATOLOGIC CHART 1

Note:

Label with a "B" any lesion biopsied or referred to physician.

P = Papilloma
N = Flat pigmented nevi
R = Raised pigmented nevi
T = Telangiectasia
K = Keratoses

Area of other noteworthy lesions should be noted and labelled.



REMARKS:

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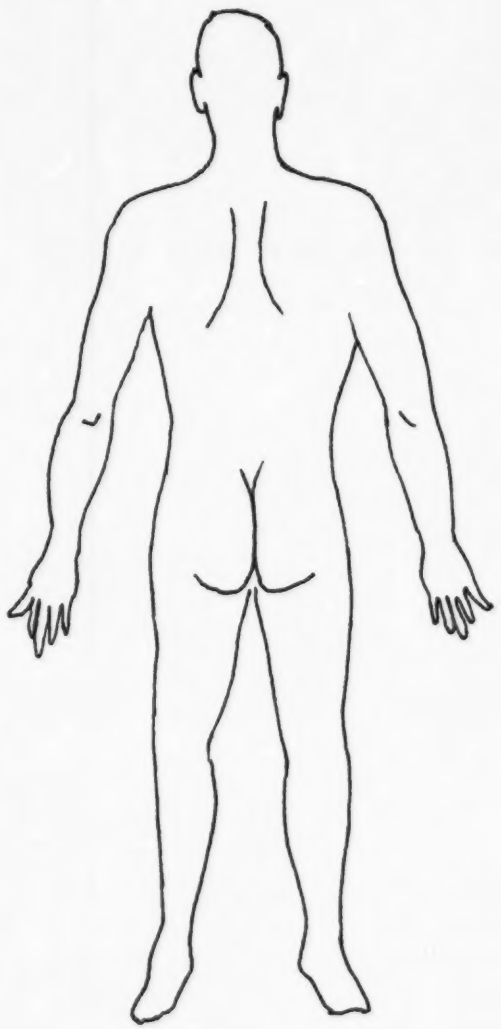
APPENDIX B-2

24 28 297

DERMATOLOGIC CHART 2



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APPENDIX B-3

24 28 297

MILLARD COUNTY ARSENIC STUDY

DERMATOLOGIST'S EXAMINATION FORM

Date _____ Case Number _____

Name _____

General Appearance

Color of:

Eyes: [ ] Brown [ ] Blue [ ] Blue Green [ ] Green

Hair: [ ] Black [ ] Dark Brown [ ] Light Brown
[ ] Red [ ] Blond

Skin: Pigmentation in non-sun exposed areas
[ ] Light Caucasian [ ] Oriental
[ ] Medium Caucasian [ ] Negro
[ ] Dark Caucasian

Hue: [ ] Pale [ ] Normal [ ] Ruddy

Amount of Scalp hair:
[ ] Normal [ ] Overabundant [ ] Scant

Skin Examination

Skin Lesions:

1. Active Keratosis: (Enter number of lesions)

Scalp _____ Arms _____

Head and Neck _____ Dorsal hands _____

Trunk (back) _____ Palms and Soles _____

Other _____

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MILLARD COUNTY ARSENIC STUDY - DERMATOLOGIST'S EXAMINATION FORM (Continued)

Skin Lesions: (continued)

2. Tumors: (Enter number of lesions)

Scalp _____ Arms _____

Head and Neck _____ Dorsal hands _____

Trunk (Back) _____ Palms and Soles _____

Other _____

Probable tumor type: (List) _____

_____

_____

3. Hyperpigmentation: (1 - 4+)

Trunk _____ Extremities _____

4. Hyperkeratosis: (Palms and Soles)

Describe _____

_____

_____

_____

5. Vascular changes - extremities _____

Describe _____

_____

_____

_____

6. Nail changes: _____

Describe _____

_____

_____

_____

7. Other abnormalities: _____

Describe _____

_____

_____

_____

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APPENDIX C

DROPPED HEAD; BEGIN SECTIONS HERE

NO._____

NAME:_____ DATE:_____

AGE:_____ SEX:_____

NERVES

	P. LAT.	D. LAT.	Δt	DISTANCE	VELOCITY	AMP/DURATION P	AMP/DURATION D	TEMP.
ULNAR (MOTOR)								
ULNAR (SENSORY)								
MEDIAN (MOTOR)								
MEDIAN (SENSORY)								
PERONEAL								
SURAL								

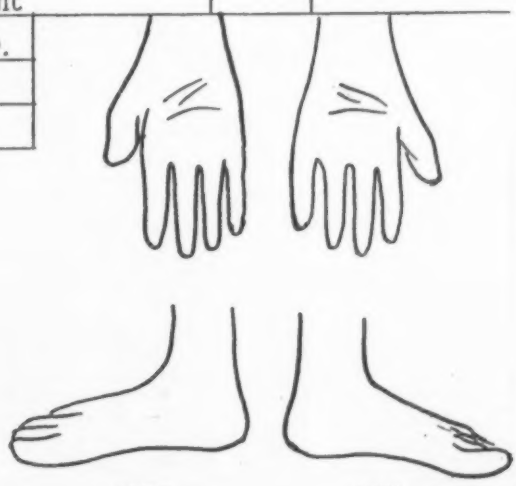
SENSORY

	POS.	VIB (0-4)	AESTH.	PAIN	TEMP.
TOES	/10		g	cm	/6
FINGERS	/10		g	cm	/6

AUTONOMIC

	COLOR	SWEAT	TEMP.
TOES			
FINGERS			

COMMENTS



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APPENDIX C-1

PATIENT'S PERSONAL HISTORY

Patient No. _____

Date _____

Confidential Record: Information contained here will not be released except when you have authorized us to do so.

Last Name	First	Middle	Birth Date	Birth Place

Address	City	State	Zip	Home Phone	Business Phone

Occupation	Medicare No.	Medicaid No.	Sex	Marital Status	Religion
			M F		

Insurance Company	Insurance No.

Person to Notify _____ Relationship _____

Address _____ Phone Number _____

Date of Last Physical Examination _____ Doctor _____

Family or Referring Physician _____ Address _____

FAMILY HISTORY		If Living		If Deceased	
	Sex	Age	Health	Age at Death	Cause
Father					
Mother					
Brothers/Sisters* *(Circle Sex)*					
	M F				
	M F				
	M F				
	M F				
	M F				
Husband/Wife					
Sons/Daughters* *(Circle Sex)*					
	M F				
	M F				
	M F				
	M F				
	M F				

*Since some names may be used for either men or women, please circle sex for each Brother, Sister, Son or Daughter.

Do you know of any blood relative who has or had: (Circle and give relationship)

Stroke	_____	Epilepsy	_____	Heart Attack	_____	Nervous breakdown	_____
Cancer	_____	Suicide	_____	Stomach ulcers	_____	Rheumatic heart	_____
High blood Pressure	_____	Migraine	_____	Kidney disease	_____	Insanity	_____
Tuberculosis	_____	Asthma	_____	Goiter	_____	Congenital heart	_____
Diabetes	_____	Hay fever	_____	Arthritis	_____		
Leukemia	_____	Bleeding tendency	_____	Colitis	_____		

PERSONAL HABITS: (Circle)

Yes No Do you regularly smoke? Cigarettes ☐ Pipe ☐ Cigars ☐ For how many years? _____

Yes No Do you usually drink over 6 cups of coffee per day?

Yes No Do you regularly drink alcohol? 1 oz. per day ☐ 2 oz. per day ☐ 4 oz. per day ☐ over 6 oz. ☐;
BEER: 1 bottle per day ☐ 2 bottles per day ☐ over 4 bottles per day ☐.

Yes No Do you have difficulty in falling asleep?

Yes No Do you awaken early in the morning without apparent cause?

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APPENDIX C-2

MEDICATIONS:

Are you presently taking any of the following medications? (Circle)

Yes	No	Aspirin, bufferin, anacin	Yes	No	Tranquilizers
Yes	No	Blood pressure pills	Yes	No	Weight reducing pills
Yes	No	Cortisone	Yes	No	Blood thinning pills
Yes	No	Cough medicine	Yes	No	Dilantin
Yes	No	Digitalis	Yes	No	Shots
Yes	No	Hormones	Yes	No	Water pills
Yes	No	Insulin or diabetic pills	Yes	No	Antibiotics
Yes	No	Iron or poor blood medications	Yes	No	Barbiturates
Yes	No	Laxatives	Yes	No	Birth control pills
Yes	No	Sleeping pills	Yes	No	Phenobarbital
Yes	No	Thyroid medicine	Yes	No	Other drugs not listed

Write in the names and year of any operations which you have had:

Name any drugs to which you are allergic:

Write in the names of any diseases you have had which required hospitalization:

Serious illnesses which you have had: (not requiring hospitalization)

Serious injuries or accidents:

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APPENDIX C-3

To be answered by WOMEN only: (Circle)

Yes	No	Are you still having regular monthly menstrual periods?	
Yes	No	Have you ever had bleeding between your periods?	When? _____
Yes	No	Do you have very heavy bleeding with your periods?	When? _____
Yes	No	Do you feel bloated and irritable before your period?	
Yes	No	Are you now on or have you ever taken the birth control pill?	When? _____
Yes	No	Have you ever had a miscarriage?	When? _____
Yes	No	Have you ever had a discharge from the nipple of your breast?	When? _____
Yes	No	Do you regularly have the cancer test of the cervix?	Date of last test _____

How many children born alive _____ How many miscarriages _____
How many stillbirths _____ How many cesarean operations _____
How many premature births _____ Any complication of pregnancy _____
Date of last menstrual period _____

To be answered by men and women: (Circle)

Yes	No	Do you frequently have severe headaches? (If yes, answer the following):
Yes	No	Do they cause visual trouble?
Yes	No	Do they occur on one side of the head?
Yes	No	Do they awaken you at night from sleep?
Yes	No	Do they feel like a tight hat band?
Yes	No	Do they hurt most in the back of the head and neck?
Yes	No	Does aspirin relieve them?

Yes	No	Have you ever fainted?	Yes	No	Have you ever had a convulsion?
Yes	No	Spells of dizziness?	Yes	No	Double vision?
Yes	No	Spells of weakness of an arm or leg?	Yes	No	Pains in ear?
Yes	No	Ringing in ears?	Yes	No	Nosebleeds?

Yes	No	Do you frequently have bleeding gums?	Yes	No	Do you frequently have a sore tongue?
Yes	No	Do you frequently have trouble swallowing?	Yes	No	Do you frequently have nausea and vomiting?
Yes	No	Do you frequently have hoarseness?			

Have you ever had shortness of breath?: (Circle)

Yes	No	Doing your usual work?	Yes	No	Which causes you to cough?
Yes	No	Climbing a flight of stairs?	Yes	No	Accompanied by wheezing?
Yes	No	Which awakens you at night?	Yes	No	Have you ever coughed blood?
Yes	No	Do you have a chronic cough?	Yes	No	Do you cough up much sputum?

Have you ever had chest pain or tightness in the chest which begins when: (Circle)

Yes	No	When exerting yourself?	Yes	No	Radiates down the arm?
Yes	No	When walking against a wind?	Yes	No	Disappears if you rest?
Yes	No	When walking up a hill?	Yes	No	Occurs only at rest?
Yes	No	After a heavy meal?	Yes	No	When walking fast?
Yes	No	When upset or excited?	Yes	No	When walking in cold weather?
Yes	No	Palpitations	If you have chest pain or tightness please explain _____		
Yes	No	Do you sleep on more than one pillow?			

Have you recently had pain in the stomach which: (Circle)

Yes	No	Occurs 1 – 2 hours after a meal?
Yes	No	Is brought on by eating fried foods, gassy foods?
Yes	No	Awakens you at night?
Yes	No	Is relieved by antacid medications?
Yes	No	Is relieved with milk or eating?
Yes	No	Occurs while eating or immediately after?
Yes	No	Is relieved by a bowel movement?
Yes	No	Loss of appetite?

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APPENDIX C-4

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If you have had a change in bowel habit recently answer the following: (Circle)			When or since when?
Yes	No	Crampy pain in the abdomen?	
Yes	No	Alternating diarrhea and constipation?	
Yes	No	Pain during or after bowel movement?	
Yes	No	Mucous in the stool?	
Yes	No	Blood in the stool?	
Yes	No	Ribbon-like stools?	
Yes	No	Black stools?	
Yes	No	Require use of strong laxatives or enemas?	

Have you had: (Circle)			
Yes	No	Burning when urinating?	
Yes	No	Loss of control of bladder?	
Yes	No	Blood in the urine?	
Yes	No	Dark colored urine?	
Yes	No	Trouble starting to urinate?	
Yes	No	Trouble holding the urine?	
Yes	No	Getting up frequently at night?	
Yes	No	Passed a kidney stone?	

Have you recently had: (Circle)			
Yes	No	Pains in calves of legs when walking?	
Yes	No	Cramps in legs at night?	
Yes	No	Pain in the big toe?	
Yes	No	Varicose veins?	
Yes	No	Phlebitis or inflamed leg veins?	
Yes	No	Swelling in the ankles?	

To be answered by MEN only: Have you ever had: (Circle)

Yes No Loss of sexual activity? For how long? _____
Yes No Treatment for genitals (private parts)?
Yes No Discharge from penis?
Yes No Hernia (rupture)?
Yes No Prostate trouble?

Describe briefly your present medical symptoms:

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